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STEREOMICROSCOPIC STUDY OF THE SURFACE OF THE LUNG

I. DESCRIPTION OF THE METHODS USED

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In 1928 capillaroscopic studies of the alveolar capillaries were made on the anesthetized dog through a thoracotomy opening.¹ In these experiments a Zeiss capillarscope was used (fig. 1). It offered a satisfactory visualization of the alveolar capillaries through the transparent virgin visceral pleura. The details of the alveolus were not distinct, and it became obviously necessary to see the saccules in more than one dimension by means of stereoscopic visualization. An opportunity for such study has been offered by the Zeiss surface stereomicroscope with a complete double lens system. This microscope may be used with the ordinary small stand, particularly for the study of smaller blocks of tissue from the lungs (fig. 2). It may be used with a larger adjustable stand also, so that the whole lung may be studied in the living or the dry state (fig. 3).

The illumination is so adjusted that light is reflected from the upper surface of the object. Use of this principle is made both in the stereomicroscope and in the capillarscope. The advantage of this type of lighting lies in the fact that objects of any size or thickness can be studied at the exposed surfaces. Microscopic examination of the surface is particularly adaptable to the study of the lung because of its sponginess and its many combinations of sacs and skeletal structures.

The microscope offers the added advantage that it can be held by the hand for microscopic study much as the telescope is held for the study of distant objects. It also has an interchangeable system of

From the Department of Surgery, College of Medicine, University of Illinois.

1. Olkon, D. M., and Joannides, M.: The Capillary Circulation of the Alveolus Pulmonalis in the Living Dog, *Arch. Int. Med.* **45**:201-205 (Feb.) 1930; Capillaroscopic Appearance of the Pulmonary Alveoli in the Living Dog, *Anat. Rec.* **45**:121-126 (March 25) 1930.

lenses and objectives, so that various magnifications may be obtained by changing either the oculars or the objectives. For small magnifications only for the study of the gross variations of the pulmonary ele-

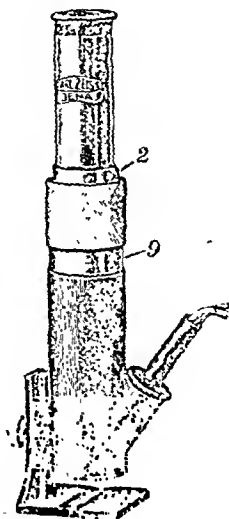


Fig. 1.—The Zeiss skin microscope, as suggested by Professor Müller of Tuebingen.

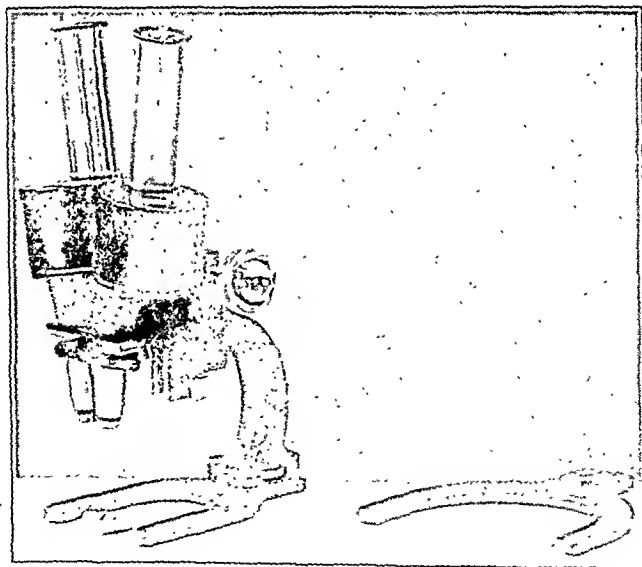


Fig. 2.—The Zeiss surface stereomicroscope.

ments, this method is satisfactory. For the larger magnifications, at which the focal point changes with even the slightest motion, the adjustable stand was found most efficient (fig. 3).

THE CAMERA

For purposes of reproduction a stereomicroscopic camera made by Zeiss (fig. 4 *A*) was used. This camera has two dark chambers and makes two stereoscopic exposures at one sitting. The system of lenses used for the microscope can be used with the camera. For better reproduction of detail the Wratten emulsion was placed on glass plates. The plates, being of an odd size, had to be made specially. For larger magnifications of the pictures I attached a magnifier to the top of the camera (fig. 4 *B*), but this procedure has not given clear pictures, especially in the greater micromagnifications.

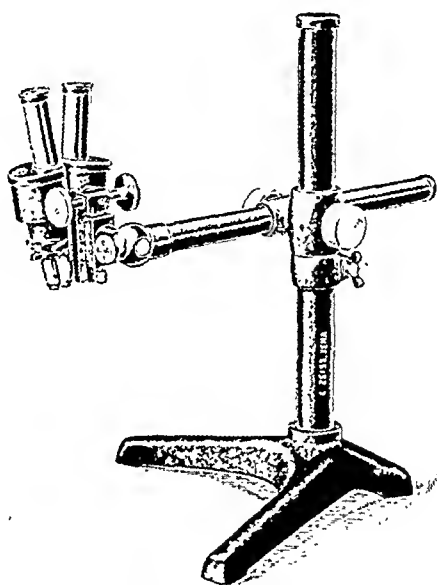


Fig. 3.—The larger adjustable stand for the study of large specimens of the lungs of anesthetized animals.

LIGHTING SYSTEM

Illumination was obtained by using a carbon arc lamp with the rays directed to the field of vision. In the living animal I wished to avoid changes due to drying by the heat of the light projected at the field. Accordingly, I either kept the part of the lung cool by soaking it with physiologic solution of sodium chloride or used a less powerful system of lighting. In this system a small electric bulb was used and the light projected to the spot by means of lenses.

STUDY OF THE LUNG IN VIVO

The specimens of lung were prepared in one of various ways, according to what I wished to study. For study of the lung in the living animal a thoracotomy with artificial respiration was sufficient. A por-

tion of the lung was taken out, and care was taken to avoid as much as possible an excessive exposure of the remaining intrathoracic organs. The exposed lung expanded and collapsed with intermittent intratracheal artificial respiration.

Because artificial respiration introduced variable factors, namely, the rate, the volume and the pressure of the blast of air, I tried to eliminate it from the study of the lung. After extensive search I noted that the lung of the alligator expands and collapses when the chest is open. This phenomenon is due to the fact that the lung is adherent to the dome of the chest and also to the diaphragm. On section of the lung in this animal, I noticed also a circular contractile tissue that aids in opening and closing the apertures to the alveolar elements of

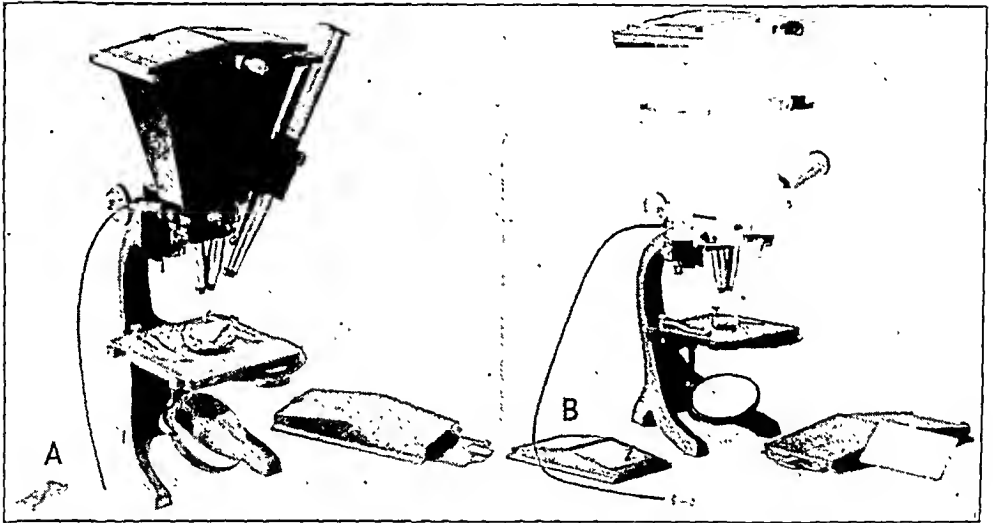


Fig. 4.—*A*, the Zeiss stereomicroscopic camera. This camera may be attached to the smaller or the larger stand. *B*, stereomicroscopic camera with a magnifier in situ.

the lung. The alligator can be easily put to sleep by means of a few drops of chloroform or ether placed on a cotton pad and pushed into its mouth.

For the study of the capillaries of the lung, the frog has given the best results. After pithing the animal, I inserted a small glass tube into the trachea and allowed just enough air to flow into the lung to produce fair distention. If too much pressure is exerted in the trachea the blood in the capillaries is squeezed into the larger vessels, and the capillaries are filled with air emboli. This occurrence causes no apparent injury to the vessels.

STUDY OF SPECIMENS OF LUNG

The ordinary pathologic or normal specimens of lung were studied after fixation with Kaiserling's solution or solution of formaldehyde. For special studies, after preliminary tying of the pulmonary vessels, I filled the bronchial tree with the fixing solution in addition to dipping and keeping the specimen in it.

In some specimens, after preliminary ligation of the vessels, I allowed air to run into the bronchial tree at a pressure just great enough to produce distention of the lung. Overdistention produced pleural bullae. Air was run into the lung until it was completely dry, and it was then divided into large blocks for study. In order to avoid overdistention the air was blown through a T tube, one end of which was attached to the lung and the other to a screw clamp. The outflow of air was regulated by tightening the screw clamp up to the point at which the optimum expansion of the lung was obtained.

For the study of the lung of a large animal, such as the cow, it was necessary to avoid decomposition of parts of it preliminary to drying. I found it more satisfactory first to fill the bronchial tree with solution of formaldehyde U. S. P. diluted 1 to 10 and then to distend the lung. Such a fixation of the bronchial and bronchiolar elements often aids in producing a sponge effect on the lung. One can then take a piece of dry lung and soak it in water, thus filling the alveoli with clear water and offering another means of study. If the lung is not treated in this manner and is only dried in the distended state, it crumples into a mass of gelatinous material when it becomes wet. The dry specimens must be handled with great care because they crumple easily. In cutting various blocks for study it is necessary to use a thin, flat, sharp knife.

ANIMAL SPONGES

Fixation of the bronchial tree with solution of formaldehyde for the production of animal sponges is practical and is a means of getting soft sponges. Because of the expense involved in their production, sponges of this type are, at least at present, not commercially practical.

PREPARATION OF PHOTOGRAPHS

The reproductions obviously must be developed in absolute darkness or under a dim blue light. Wratten films are sensitive even to red light. In order to keep the plates in their respective positions I made it a rule to draw a line with a wax pencil along the inner border of

each of the two plates. This line was drawn on the glass side, so that it could be wiped off when the positives were made. The positives were mounted on cardboard under stereoscopic vision so that proper distances and adjustments could be made. This step is most important and means the difference between successful accurate visualization and unsightly inaccurate views on the stereoscopic cards.

The Zeiss Company furnished the photographs of the microscope and of the camera.

STEREOMICROSCOPIC STUDY OF THE SURFACE OF THE LUNG

II. THE ANATOMIC AND PHYSIOLOGIC STRUCTURE OF THE NORMAL LUNG; RÉSUMÉ OF OBSERVATIONS BASED LARGELY ON STEREOMICROSCOPIC STUDY OF THE SURFACE OF LUNGS FIXED AND IN THE LIVING STATE

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This report is presented as a brief summary of the stereomicroscopic observations on the surface of the lung which I started in 1928. I have felt for some time that the ordinary sections by which the pulmonary structure is studied do not include sufficient tissue to show the structural architecture. Cellular details are easily seen from them, but the sponginess of the lung prevents determining except inferentially the grosser characteristics, interrelations and relation to the mother stem of the alveoli. By stereomicroscopic study of the surface it is possible to see an alveolus in its three dimensions and actually to study its structural, cellular and vascular detail. On first examination the worker will be amazed at the complexity of the variegated holes and strands appearing in every possible position. With sufficient patience he will discover to his pleasure and amazement a new treasure of information. It is hoped that those who undertake such a study will neither be over-enthusiastic nor become greatly discouraged, because it will take months of persistent examination before the kaleidoscope of data will begin to assume its proper classification and form.

This work was started at the surgical research laboratories of the College of Medicine of the University of Illinois. I had an opportunity in 1929 to spend some time in Europe. When in Berlin, I was fortunate in being allowed by Prof. Max Busch to study the thoracic sections prepared by Prof. Koch,¹ on exhibit in the Museum of the Pathologische Abteilung of the Reichsarbeits Ministerium. These specimens, prepared during the World War, make an excellent collection of sectional views of the lung, showing its relation to the wall of the chest and to the adjacent intrathoracic structures. Practically all types of pulmonary lesions described in textbooks of pathology are found in this collection. I have made free use of most of the sections.

From the Department of Surgery, College of Medicine, University of Illinois.

1. Koch, W.: *Thorakschnitte von Erkrankungen der Brustorganen*. Berlin, Julius Springer, 1924.

On my return to the United States, the work has been continued to date at the University of Illinois. Little has been published so far on my observations ² because the data obtained from this work appeared new and I hesitated to rush into print until I was certain of my ground. In another paper I discuss the technic in detail in the hope that some enterprising persons will carry on in this work and help supply the true picture of the structure of the lung under normal and pathologic conditions.

TRACHEA AND BRONCHI

The trachea occurs in all animals, including the amphibia. In the frog, the turtle and the alligator it ends abruptly as soon as it reaches the lung. In these animals one sees no bronchial ramifications but notices the structure of the alveoli, which will be described later. In the mammalia, the trachea and bronchi assume a characteristic architecture.

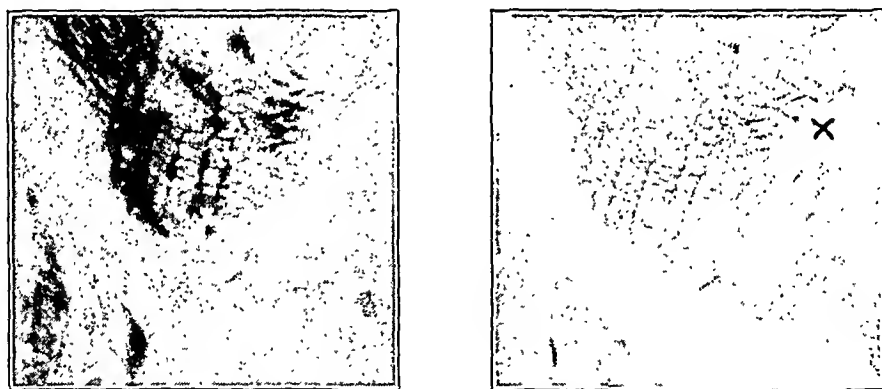


Fig. 1.—Stereomicroscopic view of the trachea. Note the longitudinal corrugations. At x the cross section of a cartilaginous ring is seen. Adjust the stereoscope to the proper focal point, and keep looking till you see depth; then study the detail.

The stereomicroscopic features of the trachea that have not been emphasized before are the trabeculations in its inner lining (fig. 1). One sees that in addition to the transverse trabeculations corresponding with the tracheal rings there are longitudinal trabeculations extending along its whole length.

The bronchi do not have any trabeculations and in my studies showed no special features not previously described. The branchings are given off at every possible angle, and the more peripheral the branches the greater is the number of the smaller branches. The angles at the branchings are generally acute (figs. 2 and 3).

2. Joannides, M.: Structure of the Normal Lung: A Surface Stereomicroscopic Study, *Arch. Int. Med.* **47**:19-23 (Jan.) 1931. Joannides, M., and Steinman, F. H.: The Mechanism of Pneumonia, *ibid.* **47**:24-27 (Jan.) 1931.

The term terminal bronchioles was assigned to denote the subdivision of the lung known as the atrium in Miller's classification.³ There is no atrium in the mammalian lung of the type that is seen in amphibia and reptiles. The terminal bronchioles have the same cellular characteristics as the alveoli. On looking into the lumen of a terminal bronchiole one sees a corkscrew-shaped tube within a tube, much like a circular staircase. In the casts made of Wood's metal or pyroxylin the terminal bronchioles appear bulbous and are made up of a series

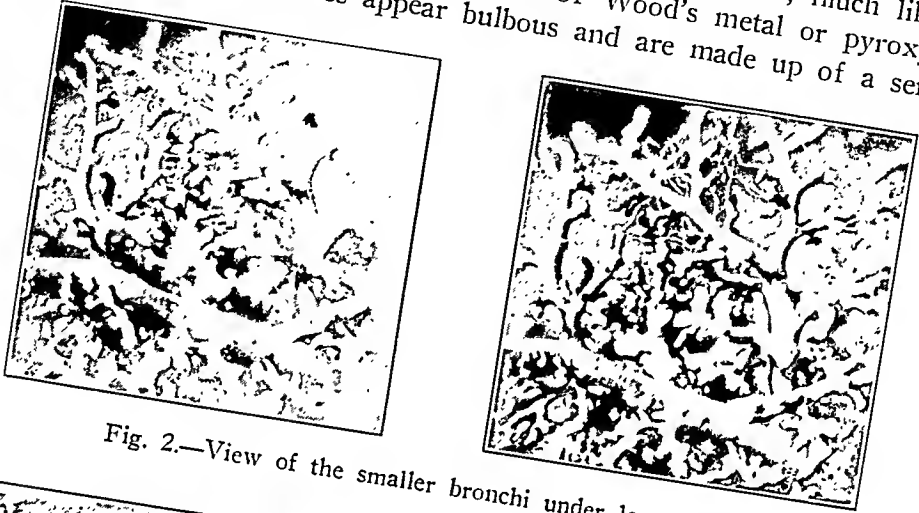


Fig. 2.—View of the smaller bronchi under low power.

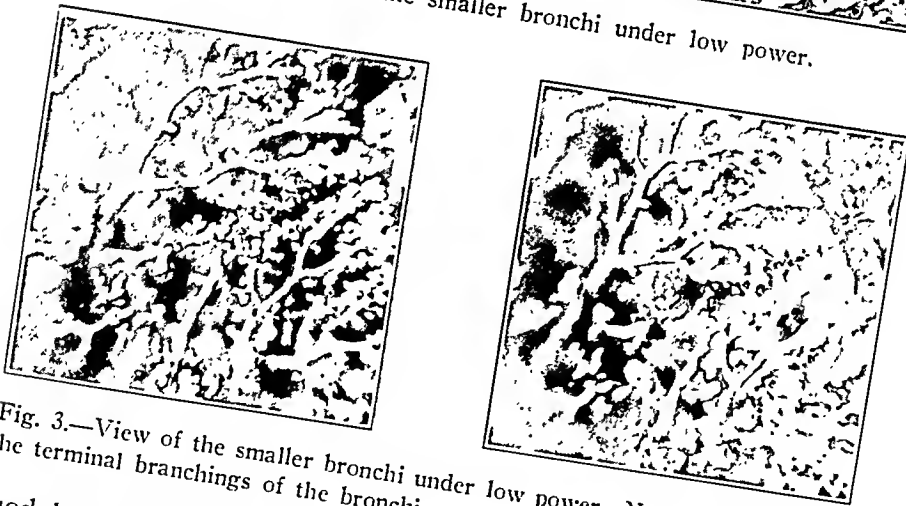


Fig. 3.—View of the smaller bronchi under low power. Note the bulbous effect at the terminal branchings of the bronchi.

of nodules arranged in more or less circular ridges. These ridges are separated by grooves, so that the general appearance of the structures suggests irregularly corrugated tubes. Each one of these circular corrugations appears to have a series of smaller cuplike grooves projecting into the wall of the terminal bronchiole. These grooves are approxi-

3. Miller, W. S.: *Anatomy of the Lungs*, in *Reference Handbook of the Medical Sciences*, ed. 4, New York, William Wood & Company, 1923, vol. 6, p. 82; *The Lung*, Springfield, Ill., Charles C. Thomas, Publisher, 1937.

mately the same size as those of the alveoli. The internal characteristics of the terminal bronchiole are those of a corkscrew-shaped tube with a bannister-like structure which represents the inner wall of the corrugated parts of the tube. Here one sees the bulbous projections into the outer wall of the "terminal bronchiole."

There is no evidence of any intercommunication between any groups of bronchi or bronchioles, except through the parent stem. My observations appear not to confirm the work of Van Allen and his associates,⁴ who have described the presence of a collateral respiration.

STEREOMICROSCOPIC VIEWS OF THE SURFACE OF THE DRY LUNGS

The comparison of the lung to a tree is quite an apt one. The trunk of the tree is analogous to the trachea. There are generally no branches along the trunk. The larger bronchi may be compared to the larger branches of the tree. The bronchi of the third and fourth order may be compared to the smaller branches of the tree. These smaller branches give off more and more smaller branches till the final branchings are seen bearing the leaves. The alveoli of the lung serve much the same function as the leaves of the tree. Each leaf is so situated that it is fully exposed to the rays of the sun. So it is with the pulmonary alveoli. Each group of alveoli is so arranged as to take advantage of every available space in the thoracic cavity. Two neighboring groups of alveoli may have their origin from fairly distant secondary or even tertiary bronchi.

At the tips of the bronchial tree in the metallic or pyroxylin casts one sees clusters of small bulbs springing out of the end of the bronchiole. These appear much like warty projections and remind one of the terminal subdivisions of a cauliflower bulb. These cauliflower-like bulbs are attached to numerous terminal bronchioles much in the manner of a cluster of grapes (fig. 3).

The stereomicroscopic appearance of the dry, fixed, moderately expanded lung is much like that of the cut surface of a dry commercial sponge (fig. 4). At first glance, one sees a large number of various-sized holes which assume round, polygonal, triangular, or oval shapes. The blood vessels and bronchi appear as larger oval or round openings and the terminal bronchioles and alveoli as the smaller openings. The bronchus and two vessels are usually found in close proximity to one another.

THE ALVEOLI

The alveoli on the cut surface appear as saccules of various shapes, namely, polygonal, oval, round or triangular. In the dry specimen two

4. Van Allen, C. M.: *Collateral Respiration*, J. Orient. Med. **15**:35-45 (Sept.) 1931; Surg., Gynec. & Obst. **53**:16-21 (July) 1931; Ztschr. f. Anat. u. Entwicklungsgesch. **98**:453-465 and 466-474, 1932.

to three honeycomb compartments are seen within the saccule of the alveolus, produced by projections arising from its wall. The terminal portions of these septums are rounded into cuplike openings. Each opening is smaller than the area of the cup itself. The edge of the septum appears thicker and is the site of a larger capillary. The stoma of the alveolus has also a cuplike opening much like those of its compartments. The mouth of the opening is somewhat thicker than the rest of the wall, and the opening itself is narrower than the rest of the saccule. Here again one sees a larger capillary. This capillary extends into the interalveolar wall and thence to the larger vessels.

When magnified 48 times, the wall of the alveolus in the dry specimen begins to appear transparent, with distinct speckles. At first glance,

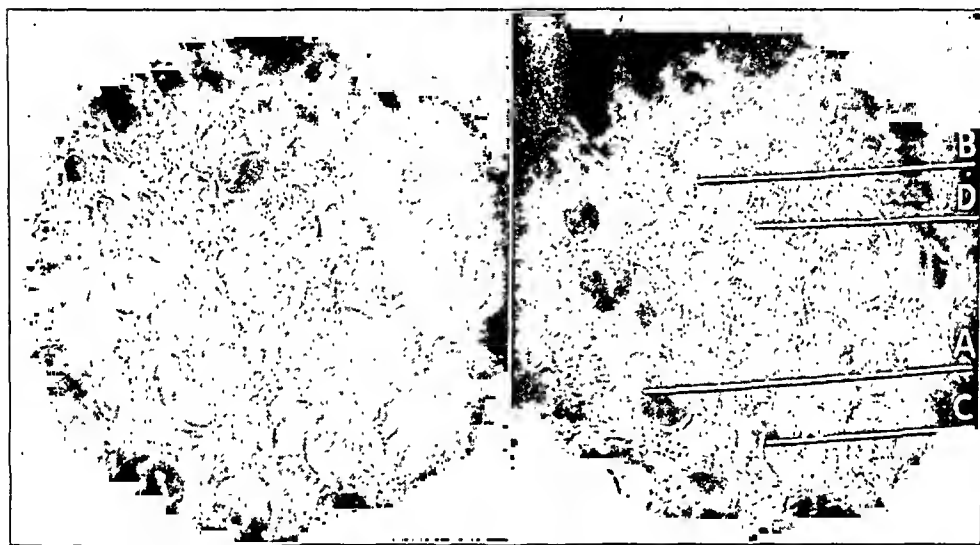


Fig. 4.—The characteristics of the alveoli. Note at the depth shown at *A* the cuplike recesses in the alveolus produced by the septums, the smaller diameter at the openings and the thin transparent wall of the alveolus. At *A* and *B* note the cross section of a terminal bronchiole and its relation to the alveoli. At *A* and *C* note the denser capillary of the cut alveolus whose terminal bronchiole originates from below. At *A* and *D* note some of the finer details of the thin alveolar wall.

one gets the impression that the alveolar wall is made up of a series of grooves and ridges, irregular in shape. On more careful examination, the ridges are seen to be the sites of the smallest possible capillaries, whose lumens allow only one red cell to pass through at a time. These capillary beds, being denser than the alveolar wall adjacent to them, are more refractive, and therefore one gets the impression of speckles between the ridges. The alveolar wall between the capillaries appears more translucent and sievelike. It is probably for this reason that pores have been previously described. I have not seen any such pores in

any specimens of normal lungs even when the lungs were overdistended to a capacity larger than that of the thoracic cavity (maximum visceral pleural capacity).

ALVEOLAR CAPILLARY CIRCULATION

The capillary circulation of the pulmonary alveolus was studied in the anesthetized alligator and in the pithed frog. The frog's lung when exposed had to be kept distended and allowed to collapse intermittently in order to get accurate readings. Care was taken not to overdistend the lung and squeeze air from the pulmonary sacculi into the capillaries. Such overdistention can be easily accomplished even in the mammalia without causing any apparent injury to the alveolar wall itself.⁵ The alligator's lung has a capacity of contracting and expanding without artificial inflation and offers a better means for the study of the capillary circulation of the alveolus. In order not to cause a tear in the lung the visceral pleural surface is studied for this purpose. It must be emphasized, however, that the alveolar wall is to be focused into the visual field and not the transparent pleural wall.

The one cell capillaries arise from the multiple cell capillary located in the periphery of the alveolar wall. These capillaries follow a rather tortuous course and terminate at the opposite multiple cell capillary. There is no apparent collateral ramification of the one cell capillaries. The alveolar wall is literally studded with them. The blood is seen to flow in one direction from one larger capillary, through the one cell capillaries, to that on the opposite side. I have not noticed any reverse flow of blood cells. At first glance, the course of the blood cells appears much like the wavy motion which is seen on the surface of a wheat field when a gentle wind blows over the plants. When the lung is fully distended or contracted, the flow becomes retarded. It is accelerated coincident with the process of distention or contraction. Similarly, with digitalization of the cardiac muscle, the flow of blood becomes retarded so that one can see the actual course a red blood cell follows in these capillaries. The blood cells are seen taking a rather tortuous, zig-zag course, always in the same one cell capillary, and finally reaching the larger capillary on the opposite side. The one cell capillaries appear more straight when the lung is distended and more tortuous when it is contracted (fig. 5).

I have not as yet made any study of the lymph and nerve supply of the lung. I am trying to find appropriate methods or differentiating

5. Joannides, M., and Tsoulos, G.: The Etiology of Interstitial and Mediastinal Emphysema: Experimental Production of Air Embolism, Acute Spontaneous Pneumothorax, Acute Pneumoperitoneum, Interstitial Mediastinal and Retroperitoneal Emphysema, *Arch. Surg.* **21**:333-339 (Aug.) 1930.

vital status so that I can trace these two important attributes of the lung in the living animal.

PLEURAL SURFACE OF THE LUNG

The pleural surface of the lung yields no new observations. The checkered appearance of the human lung, especially in the presence of anthracosis, is well known to all. This appearance is most noticeable in the lungs of cattle and least noticeable in those of sheep. The lobulations of the pleural surfaces are of definite importance teleologically. The pleural projections into the lobules of the lung prevent the rupture or injury of large portions of the lung⁶ (fig. 6).

One fact of importance must be emphasized because of its clinical applications. At various areas one sees a bulla corresponding to the lumen of the underlying bronchiole. Careful study of such areas reveals

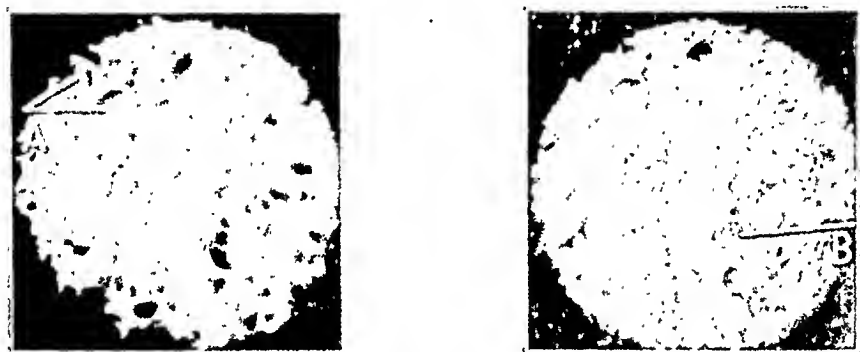


Fig. 5.—Distribution of pulmonary vessels. The vessels are injected and emphasize detail in the smaller branches. At *A* the characteristics of the inner surface of the bronchus are shown. At *B* the characteristics of a terminal bronchiole are shown.

that here and there a bronchiole ends abruptly underneath the pleura without any alveolar subdivisions. It is frequently in areas such as these that injury to the lung occurs when there is a sudden increase of intrabronchial air pressure. The pleura ordinarily acts as a water-tight and air-tight sheath of the lung. It can be peeled off easily if one exerts in the lung of a dog or in an excised human lung a sudden pressure of 100 mm. of mercury in repeated blasts of air. The pleura loses its adhesive power, and a bulla forms which enlarges as far as the boundaries of the pulmonary lobules. If the pressure is maintained long enough (thirty to sixty seconds) the pleural bulla may rupture and cause a spontaneous pneumothorax.⁶

6. Joannides, M.: Protective Power of the Pleura, *Am. J. M. Sc.* **180**:833-836 (Dec.) 1930.

REPAIR OF PULMONARY INJURIES

The lung contains a thick yellow gelatinous substance which acts as an adhesive agent in case of minor injuries. Injury to the lung without injury to any larger bronchi or vessels causes this substance to fill in the space and promptly stop the air from leaking out of the injured part. In a few minutes it appears as a thick cover so that bubbles of air can be seen underneath it. In the dog one can easily demonstrate the presence of this substance by making a stab wound in the lung. The air now begins to leak through, and along with it is noticed this substance, mixed with blood. To hasten the cohesion one may take the two cut portions, approximate them and exert a slight pressure with the thumb and index finger. Within thirty to sixty seconds the lung appears again completely air tight and water tight, as if no injury had occurred.

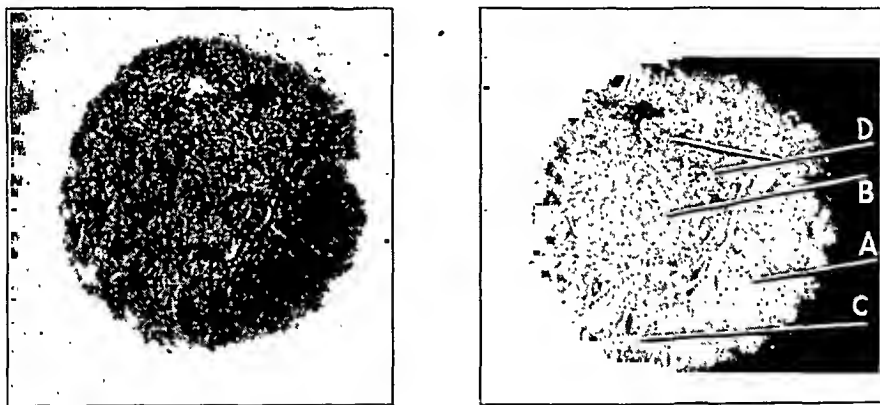


Fig. 6.—The characteristics of an interlobular septum. At *A* note the particles of coal embedded in the wall of the alveolus. At *B* note the characteristics of the alveolus. At *C* note the comparative greater thickening at the mouth of the sacule. At *D* note the relatively loose relationship of the alveolar elements to the interlobular septum.

EXTERNAL RESPIRATION IN THE ALLIGATOR'S LUNG

The presence of a circular contractile ring in the atrium of the alligator's lung has been noticed. This ring functions in connection with external respiration. It reaches its maximum closure at the end of inspiration and then gradually dilates and reaches its maximum dilatation at the height of expiration and the beginning of the inspiratory phase.

EFFECT OF CARDIAC CONTRACTIONS ON THE VOLUME OF THE LUNG

Observation of the lung through a thoracoscope and also through a fluorescent roentgen screen reveals an interesting phenomenon. The

whole lung expands slightly at a moment coincident with the cardiac systole. This increase in pulmonary volume disappears during the diastolic phase of the cardiac cycle. One gets the impression of a pulsating lung coincident with the cardiac contractions. Under the fluoroscope the pulsation becomes obvious when the lung is partially collapsed with artificial pneumothorax and the intrapleural pressure is negative. It may be possible by studying the amount of intrapleural pressure necessary to eliminate this pulsation as seen in the fluoroscopic screen or on a recording drum to find a clinical method for studying the changes of pressure in the pulmonary circulation.

SUMMARY

1. A study of the normal structure of the lung, both in the fixed and in the dried human specimens and in the living animal, such as the frog, the turtle, the alligator and the dog, shows that the lung presents the same fundamental architecture in all these animals. Variations consist primarily of the greater complexity in the mammalia. The frog's lung may be looked on as a magnification of the general structure of an alveolus. The relation of the atrium to the terminal bronchiole can be noticed definitely in the lung of the turtle.

2. Casts of the bronchial trees of mammals show that the greatest number of ramifications are given off by the smaller branches of the bronchial tree. These findings suggest an analogy to the branching of large shade trees.

3. The terminal bronchiole, or atrium of Miller's classification, is seen as a corkscrew-like cochlea-shaped tube with a circular cup-shaped groove enclosed within the various corrugations of the wall. There is a gradual transition in the bronchial tree from the tracheal type of structure in the larger bronchi to the alveolar type in the terminal bronchioles (figs. 7 and 8).

4. The pleural surface of the lung offers an opportunity for the study of the pulmonary alveolus. The pleura is transparent and easily placed out of focus.

5. The normal alveolus is a small round, oval, triangular or polygonal sac with two or more compartments produced by septums arising from the alveolar wall. The alveolar stoma is smaller than the sac, both in the alveolus and in its compartments.

6. The alveolar capillaries flow in one direction without any back flow. There is no apparent collateral capillary circulation. The capillaries follow a tortuous course along the surface of the alveolar wall and reach the larger capillary on the opposite end of the wall.

7. The visceral pleura acts as a loosely adherent air-tight and water-tight covering of the lung, and its boundaries are those of the lobules.

8. The lung contains an adhesive substance that heals its minor injuries.

9. Some bronchioles may be seen to terminate abruptly underneath the visceral pleura. I believe that this condition is frequently the cause of spontaneous pneumothorax.

10. A diligent search for collateral respiration and the presence of alveolar pores⁷ has failed so far to show me the existence of either one or the other.

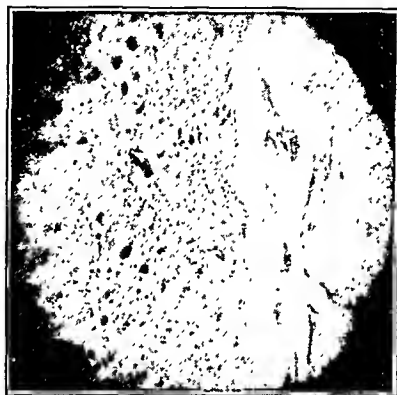
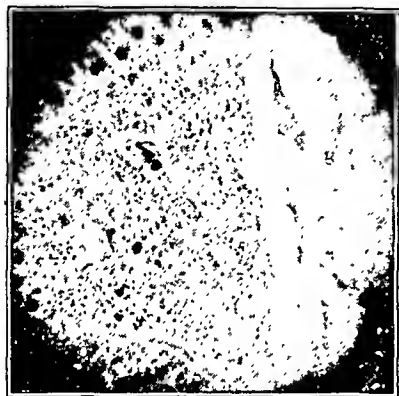


Fig. 7.—Longitudinal section of a bronchiole. Note the gradual change from bronchial to alveolar architecture.

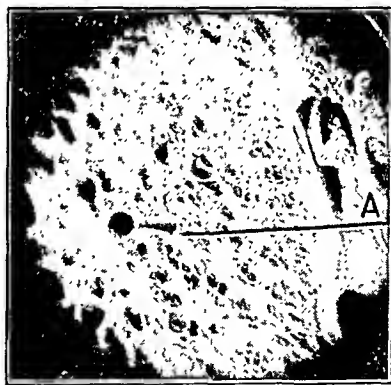
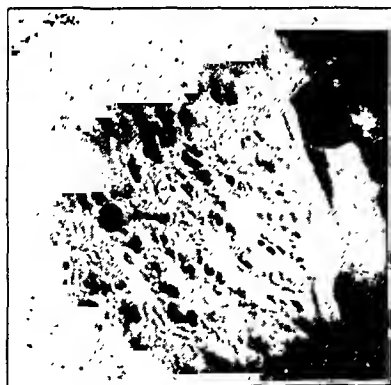


Fig. 8.—Section made in a case of carcinoma of the lung. Pulmonary implantations of cancer originating in the mediastinum. Note the disappearance of the alveolar elements and the transfer of the respiratory function to the terminal bronchioles.

11. W. S. Miller came closest to describing the actual structure of the alveolus through his reconstructional studies.

7. Macklin, C. C.: Alveolar Pores and Their Significance in the Human Lung. Arch. Path. **21**:202-216 (Feb.) 1936.

CHRONIC APPENDICITIS

IS IT A CLINICAL ENTITY?

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This study was undertaken in an attempt to determine whether or not there is such a clinical entity as chronic appendicitis. The subject has been approached from the following three angles: First, the pathologic changes in appendixes supposed either before or after the operation to have been the cause of symptoms have been compared with the changes in those which apparently had never been the cause of symptoms. Second, the incidences of pathologic changes in appendixes supposed to have been the cause of symptoms have been determined according to symptoms, physical findings, laboratory findings, sex and age. Third, the percentages of the patients followed up who remained free from symptoms have been determined according to the pathologic change found in the appendix and the other classifications just listed.

In a study¹ made of the appendix in cases in which nothing in the history or physical findings indicated any present or past disease of that structure, in two thirds of the cases there was found to be definite pathologic change (table 1). The incidences of inflammatory changes in the appendix for the total number of cases in which it was not the cause of symptoms, both when some other inflammatory lesion existed in the abdomen and when no other inflammatory lesion was noted, are also listed. The latter incidence was chosen for purposes of comparison in this study, as it was considered to be the nearest approach to the expectation of pathologic change in the appendix when the patient has been erroneously operated on for chronic appendicitis. Reference will be made to these figures as a standard for comparison throughout the paper.

The time covered was the same in the two series of cases, the eleven year period from 1925 to 1935. The cases studied included those of all patients operated on within this time in the wards at St. Luke's Hospital whose symptoms were attributed, either before or after the operation, to

From the Surgical Services of St. Luke's Hospital.

Presented before the Hospital Graduates Club, March, 25, 1937.

1. Shelley, H. J.: The Incidence of Asymptomatic Pathologic Conditions in the Appendix, Based on Study of 2,065 Consecutive Incidental Appendectomies, *Arch. Surg.* **35**:621 (Oct.) 1937.

a nonspecific chronic inflammatory lesion in the appendix. Eight hundred and eighty-one appendectomies met these requirements. For clarity, the various percentages throughout the paper have been stated as the nearest whole number, unless the percentages were so small that accurate comparisons could be made only by retaining the fraction. When comparisons were made of the incidences of pathologic change in various groups, these incidences were calculated on the total number of appendixes in each group. The incidences in relation to the total number of cases studied are given in the tables as well as the percentages of follow-up cures.

TABLE 1.—*Incidence of Inflammatory Change in the Appendix Without Symptoms or Physical Findings*

	Total Cases	Total Without Inflammation*	Normal*	Atrophic*	Total with Inflammation*	Simple Chronic Appendicitis*	Total with Marked Changes*	Chronic Catarrhal Appendicitis*	Chronic Exudative Appendicitis*	Acute Appendicitis*	Chronic Obliterative Appendicitis with Infiltration*	Chronic Obliterative Appendicitis without Infiltration*	Chronic Periapendicitis*	Acute Periapendicitis*
Appendixes studied.....	1,890	37	33	3.9	63	30	33	4.3	8.3	1.8	5.6	9.7	1.6	1.2
Inflammation elsewhere in the abdomen.....	751	32	29	3.1	68	34	35	3.6	8.4	1.3	6.3	8.5	3.6	3.1
No inflammation elsewhere in the abdomen†..	1,139	41	37	4.3	59	28	31	4.8	8.3	2.0	5.2	10.5	0.4	0.0

* All the statistics are stated as the incidence per cent of the total number in each group.

† The incidence when no inflammation was present in the abdomen other than in the appendix (lower line of figures) is considered as representing most closely the findings to be expected when the condition in the appendix is not the cause of the patient's symptoms.

The percentages of follow-up cures were established as follows: A total of 704, or 80 per cent, of all the patients were followed for an average of twelve and a half months. Of these patients, 87 per cent had no return of the symptoms which were the indications for their operations. The percentages of cures stated in the tables were calculated by dividing the number of persons having no return of their preoperative symptoms by the total number followed in each group. For the larger groups, the resulting figures may be considered satisfactory for purposes of comparison. When but a few cases fall within a group, the percentage of follow-up cures can be taken as only an indication of the success of the operation.

MICROSCOPIC PATHOLOGIC OBSERVATIONS

Listed in table 2 are the appendixes according to microscopic pathologic changes; for each group the incidence, the comparable incidence when no symptoms were noted and the percentage of follow-up cures

are given. The pathologic processes other than nonspecific inflammatory changes or their absence will be discussed later. A comparison of the incidences of microscopic pathologic change in the presence and in the absence of symptoms is presented graphically in chart 1 *A*. Only 28 per cent of the patients showed no inflammatory change, as compared with 41 per cent in the absence of symptoms. This difference was due entirely to the decrease in the incidence of normal appendixes from 37 to 24 per cent. All appendixes which were normal, relatively normal or without definite pathologic change were listed as normal. The incidence of atrophic appendixes did not vary, being 4 per cent whether

TABLE 2.—*Incidence and Follow-Up Cures According to Microscopic Pathologic Observations**

	Appendixes	Incidence, per Cent	Standard Incidence†	Per Cent Cured
No microscopic examination.....	6	0.7	...	100
Mucocele.....	2	0.2	0.2	100
Diverticulum.....	2	0.2	0.1	100
Lymphoid hyperplasia.....	1	0.1	0.0	...‡
Tuberculosis.....	2	0.2	0.3	100
Tumors.....	1	0.5	0.3	100
Total without inflammatory change.....	247	28	41	80
Normal.....	213	24	37	81
Atrophic.....	34	4	4	74
Total with inflammatory change.....	623	72	59	89
Simple chronic appendicitis.....	218	24	28	90
Total with marked changes.....	405	47	31	89
Chronic catarrhal appendicitis.....	54	6	5	91
Chronic exudative appendicitis.....	235	27	8	87
Chronic obliterative appendicitis with infiltration.....	84	10	5	92
Chronic obliterative appendicitis without infiltration.....	32	4	11	85
Total.....	881§	100		87

* These figures are more readily studied in chart 1.

† The incidence in cases which involve no history or physical findings indicating disease in the appendix is regarded as standard.

‡ No follow-up was made in this case.

§ Nine appendixes fall within two classifications each.

symptoms were present or not. This is somewhat surprising, as this condition is probably due largely to pressure, which might well be expected to cause symptoms in the right lower abdominal quadrant.

As contrasted to the foregoing observations, 72 per cent showed some type of inflammatory change—an increase from 59 per cent in the absence of symptoms. Simple chronic appendicitis was found in only 24 per cent of the cases, as compared with 28 per cent when symptoms were not noted. Therefore, the entire increase in incidence of inflammatory changes was due to the increase in the incidence of marked changes, 47 per cent as compared to 31 per cent. This increase was not uniform in the various types of change considered under the classification of marked changes. The incidence of chronic catarrhal appendicitis presented practically no variation, 6 per cent as compared to 5 per cent. The incidence of chronic exudative appendicitis was more

than tripled, from 8 to 27 per cent, while that of chronic obliterative appendicitis with infiltration was doubled, from 5 to 10 per cent. That the increased incidence of the two most active and extensive types of inflammation should account for the total increase in the incidence of inflammatory changes in the appendix is a particularly interesting point. The incidence of chronic obliterative appendicitis without infiltration was lowered, 4 per cent as compared with 11 per cent. This is a completely healed process without inflammation remaining.

The percentage of follow-up cures according to the types of pathologic change observed microscopically in the appendix are presented graphically in chart 1 *B*. The natural expectation is that the lowest

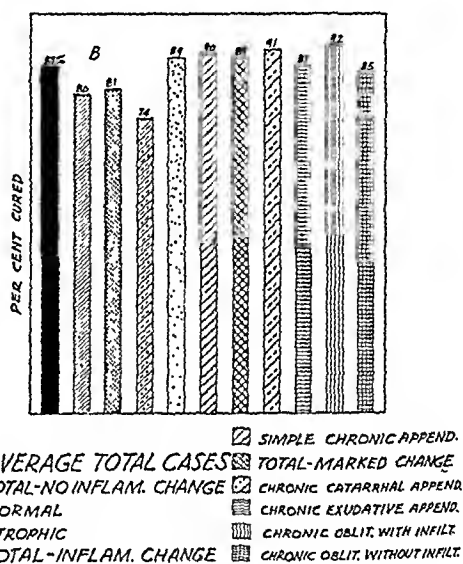
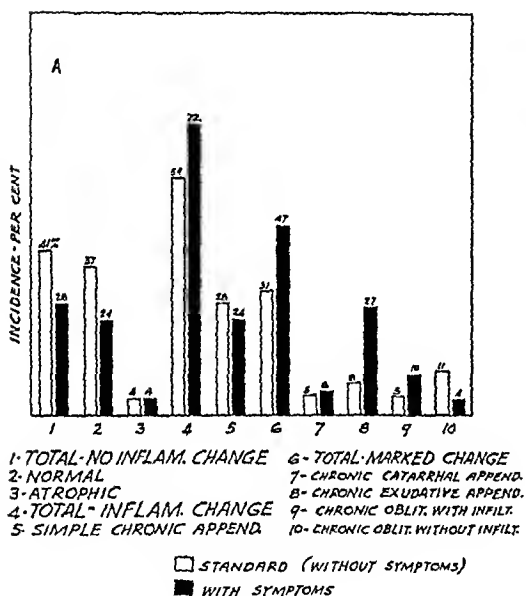


Chart 1.—*A*, comparison of the incidence of inflammatory changes in the appendix in the presence and in the absence of symptoms. The increase of the incidence of appendixes showing inflammatory changes in the presence of symptoms attributed to the appendix is definitely shown. In cases of chronic obliterative appendicitis without infiltration, which is a completely healed process, a marked decrease in the percentage showing symptoms is found. *B*, percentages of follow-up cures according to the pathologic condition observed in the appendix. A greater percentage of follow-up cures is found in cases in which inflammatory changes were present. Of this group, the lowest percentage of cures is found in cases of chronic obliterative appendicitis without infiltration. That is as expected, but one would anticipate that the highest percentage would be found in cases of chronic exudative appendicitis.

percentage of follow-up cures would be found in the cases in which the appendix was without inflammatory change. This is borne out by the figures, 80 per cent for these cases as compared with 89 per

cent for those in which inflammatory change was presented. The proportion of follow-up cures in the cases in which the appendix was normal was 81 per cent. The reason that the difference was not greater will become apparent when these figures are broken down according to gross pathologic change. Again it is surprising that the cases involving atrophic appendixes not only showed no increase in the percentage of follow-up cures, as compared with those in which the appendix was normal, but that the lowest proportion of cures, 74 per cent, was found in this group.

In cases involving the various types of inflammatory change, there was a fairly uniformly high percentage of follow-up cures, regardless of the degree of deviation from the standard incidences or the severity of the inflammatory change. In cases of chronic exudative appendicitis, the lesion which presented the greatest increase in incidence over the standard and represents the most marked type of inflammatory change, the proportion of cures was only the average, 87 per cent. In cases of chronic obliterative appendicitis without infiltration, though the incidence of the condition is much less than the standard, the proportion of cures was the lowest; but this figure, 85 per cent, was only 2 points less than the average. The proportions of cures in cases of simple chronic appendicitis (90 per cent), chronic catarrhal appendicitis (91 per cent) and chronic obliterative appendicitis with infiltration (92 per cent) were all improved over the general average, of 87 per cent.

GROSS PATHOLOGIC CHANGES

In the study of gross pathologic change only adhesions and fecaliths were considered. Variations in the incidences of microscopic pathologic change according to gross pathologic change were found in several respects (table 3). Normal appendixes occurred more frequently in the presence of adhesions than in the presence of fecaliths, the incidence being 26 per cent as compared with 20 per cent. The incidence of atrophic appendixes in the presence of fecaliths, 6.5 per cent, was more than double that in the presence of adhesions, 3 per cent, and nearly double that when neither was present, 3.6 per cent.

The total incidence of inflammatory changes was practically the same whether adhesions, fecaliths or neither was present. However, the incidence of simple chronic appendicitis was increased to 26 per cent in the presence of adhesions and 30 per cent in the presence of fecaliths, as compared with 22 per cent when neither was present. A slight decrease in the total incidence of marked changes was found in the presence of both adhesions and fecaliths, 45 and 44 per cent, respectively, as compared with 49 per cent when neither was present. The incidence of chronic catarrhal appendicitis presented no changes. That of chronic

exudative appendicitis was less in the presence of adhesions, 22 per cent, than when neither was present, 29 per cent, while in the presence of fecaliths there was an increase to 32 per cent. Changes occurred in the opposite direction and were even more marked in the incidence of chronic obliterative appendicitis, both with and without infiltration: The incidence of the former was 13 per cent with adhesions, 9 per cent with neither and 4.5 per cent with fecaliths; that of the latter, 5.2 per cent with adhesions, 3.6 per cent with neither and 0.6 per cent with fecaliths. The incidences of microscopic pathologic changes when neither adhesions nor fecaliths were present conformed closely to the averages for the total number of cases studied.

TABLE 3.—*Incidence of Inflammatory Change in the Appendix According to Gross Pathologic Observations**

	Total Cases	Total without Inflammation	Normal	Atrophic	Total with Inflammation	Simple Chronic Appendicitis	Total with Marked Changes	Chronic Catarrhal Appendicitis	Chronic Exudative Appendicitis	Chronic Obliterative Appendicitis with Infiltration	Chronic Obliterative Appendicitis without Infiltration
Standard†.....	41	37	4.3	50	28	31	4.8	8	5.2	10.5	
Adhesions.....	329	29	26	3.0	71	26	45	5.9	22	13.0	5.2
Fecaliths‡.....	154	27	20	6.5	73	30	44	5.9	32	4.5	0.6
Neither.....	387	29	25	3.6	71	22	49	6.7	29	9.0	3.6
Total.....	870	28	24	3.9	72	24	47	6.2	27	9.7	3.7

* Atrophic appendixes show a marked increase in incidence in the presence of fecaliths, as does chronic exudative appendicitis. Chronic obliterative appendicitis with and without infiltration and chronic exudative appendicitis present a marked increase in incidence in the presence of adhesions.

† The incidence in cases which involve no history or physical findings indicating disease in the appendix is regarded as standard.

‡ Under this heading are included all appendixes containing fecaliths alone and those with fecaliths and adhesions together.

To summarize: Adhesions occurred more often in the presence of chronic obliterative appendicitis and with more than the proportionate number of normal appendixes; fecaliths, on the other hand, were associated particularly with atrophic appendixes and with chronic exudative and simple chronic appendicitis.

Adhesions about the appendix were found at 38 per cent of the appendectomies, fecaliths alone or with adhesions at 18 per cent and neither at 44 per cent (table 4, chart 2). The percentages of follow-up cures were good when adhesions were present and did not vary appreciably with the extent of inflammatory change, the figure being only slightly lower when no inflammation was present. When fecaliths were present, the findings were similar. However, when neither was found,

the cures remained good in the presence of inflammatory change but dropped to the lowest figure, 74 per cent, when this condition also was absent.

HISTORY AND SYMPTOMS

Nearly all of the patients were operated on because of one or more attacks of pain in the right lower abdominal quadrant. A few had had symptoms elsewhere in the abdomen, but after an exploratory oper-

TABLE 4.—*Incidence and Follow-Up Cures According to Gross Pathologic Condition*

	Total Cases	Incidence, per Cent	Per Cent Cured				Entire Group
			Inflammation in Appendix				
			None	Slight	Marked	Total	
Adhesions.....	331	38	87	91	88	90	89
Fecaliths*.....	156	18	85	94	90	91	89
Neither.....	394	44	74†	88	90	89	85
Total.....	881	100	80	90	89	90	87

* Under this heading are included all appendixes with fecaliths alone and those with fecaliths and adhesions together.

† The low figure for follow-up cures when no adhesions, fecaliths or inflammatory changes were present is outstanding.

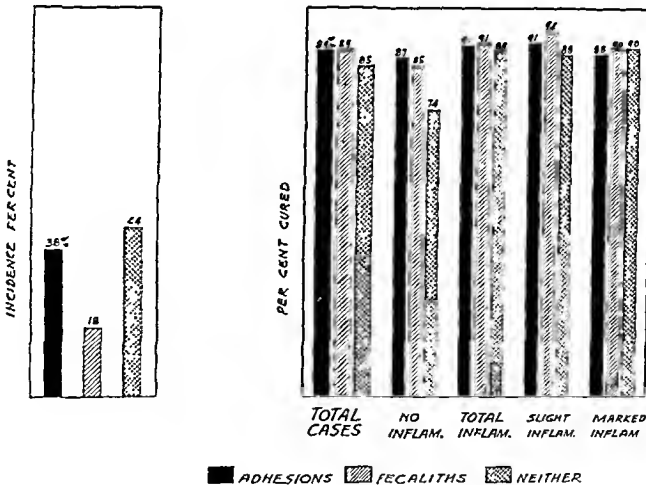


Chart 2.—Incidence and percentages of cures according to the gross pathologic condition. The increased percentage of follow-up cures in the presence of either adhesions or fecaliths is shown. In the absence of inflammatory changes, the presence of either of these two conditions brings the percentages of follow-up cures practically to that of the average of all the cases studied.

ation the symptoms were attributed to the appendix. Only 24 per cent were operated on in or following the first attack, while 45 per cent gave a history of multiple attacks over a period of one year or less and 31 per cent over more than a year (table 5, chart 3). The per-

centages of follow-up cures were remarkably high when the attacks were multiple and not extended over a longer period than one year. This was uniformly true regardless of the presence, absence or degree of inflammatory change. The lowest proportion of cures, 78 per cent, occurred when the operation was done during or following the first attack, and only moderate improvement resulted—cures in 82 per cent of the cases—when the history revealed multiple attacks over periods greater than one year. In both of the last two groups fewer cures

TABLE 5.—Incidence and Follow-Up Cures According to the Time Covered by the Attacks

	Total Cases	Incidence, per Cent	Per Cent Cured				Entire Group
			Inflammation in Appendix				
			None	Slight	Marked	Total	
First attack.....	213	24	63	89	79	82	78
Multiple attacks							
One year or less.....	392	45	95	96	97	97	96
Over one year.....	276	31	69	83	87	86	82
Total.....	881	100	80	90	89	90	87

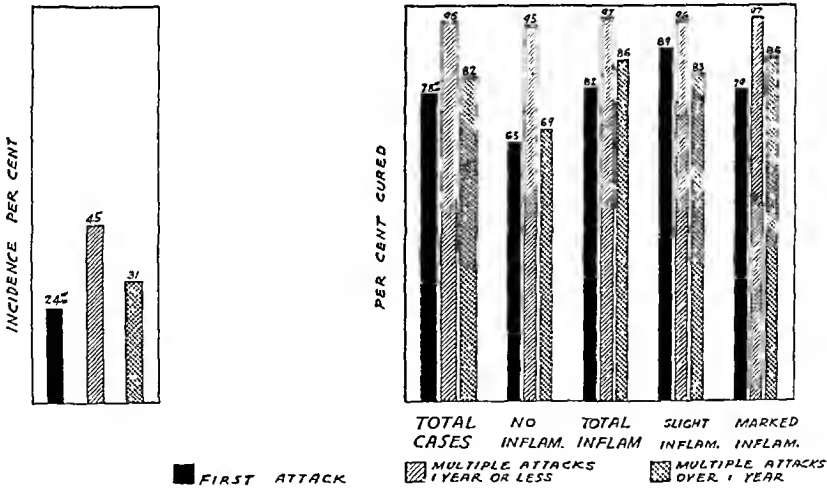


Chart 3.—Incidence and percentages of cures according to the time covered by the attacks. A uniformly high percentage of follow-up cures is found when the history indicates multiple attacks within a year, notwithstanding the presence, absence or degree of inflammatory changes. When the history indicates only one attack, the percentages of follow-up cures are the lowest throughout but vary according to the presence or absence of inflammatory changes.

resulted when no inflammatory change was found, 65 and 69 per cent, respectively. Curiously, however, the variation from the incidences of microscopic pathologic change in the absence of symptoms (table 6, chart 4) is exactly opposite to the percentage of cures. This is slight

although uniform. Chart 4 has been arranged to show this comparison by placing the groups in descending order according to the percentage of cures, i. e., those never having had symptoms, those having had multiple attacks for one year or less, those having had multiple attacks

TABLE 6.—Incidence of Inflammatory Change in the Appendix According to Time Covered by the Attacks

	Total Cases	Total without Inflammation	Normal	Atrophic	Total with Inflammation	Simple Chronic Appendicitis	Total with Marked Changes	Chronic Catarrhal Appendicitis	Chronic Exudative Appendicitis	Chronic Obliterative Appendicitis with Infiltration	Chronic Obliterative Appendicitis without Infiltration
Standard*.....	41	37	4.3	59	23	31	4.6	8	5.2	10.5	
First attack.....	209	23	21	3.9	75	26	49	7.2	27	10.0	5.3
Multiple attacks—one year or less.....	330	30	26	4.8	70	26	44	5.4	26	9.6	3.1
Multiple attacks—over one year.....	271	25	25	2.6	72	23	49	6.6	29	9.6	3.3
Total.....	570	23	24	3.9	72	24	47	6.2	27	9.7	3.7

* The incidence in cases which involve no history or physical findings indicating disease in the appendix is regarded as standard.



Chart 4.—Incidence of inflammatory changes according to the time covered by the attacks. With one exception the group of cases in which a history of multiple attacks within a year was given shows an incidence of pathologic change nearest to that found when no symptoms had been attributed to the appendix. Only in the group comprising cases of chronic obliterative appendicitis without infiltration does the expected variation occur.

for more than one year and those submitted to operation during the first attack. Nausea and vomiting were mentioned in 66 per cent of the histories studied and reported as absent or not mentioned in 34 per cent

(table 7, chart 5 *A*). No definite relation was evident between its presence and the incidences of inflammatory changes (table 8), although the percentage of follow-up cures was slightly increased in its absence (table 7, chart 5 *A*). Constipation was mentioned in 42 per cent of the histories and reported as absent or not mentioned in 58 per cent (table 9, chart 5 *B*). In the cases in which the history was negative in this respect, a slight but definite increase of the incidences of inflammatory changes was found (table 10, chart 6). An even greater increase

TABLE 7.—Incidence and Follow-Up Cures According to a History of Nausea and Vomiting

	Total Cases	Incidence, per Cent	Per Cent Cured
Nausea and vomiting.....	580	66	86
None*.....	301	34	89
Total.....	881	100	87

* This classification includes all histories in which nausea and vomiting were said not to have occurred or were not mentioned.

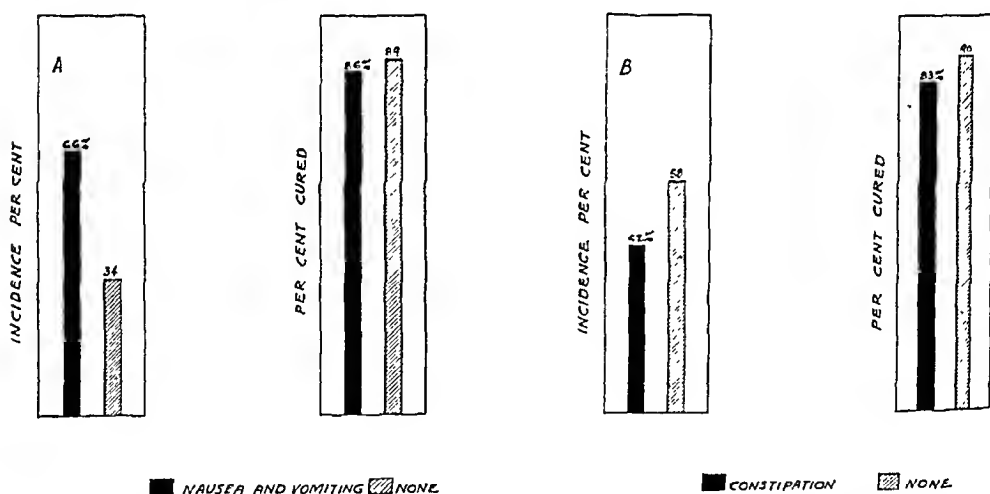


Chart 5.—Incidence and percentages of cures according to a history of (*A*) nausea and vomiting or (*B*) constipation.

in the percentage of follow-up cures occurred in the absence of the history of constipation, 90 per cent as compared to 83 per cent (table 9, chart 5 *B*). No appreciable variations were found according to the degree of inflammation present.

PHYSICAL FINDINGS

One of the most interesting sets of facts appeared in the study of the incidences of microscopic pathologic change according to physical findings and their correlation with the percentages of follow-up cures.

When tenderness was present in sites other than the right lower abdominal quadrant, the incidences of inflammatory changes checked with or approached closest to those found in the absence of symptoms and physical findings (table 11, chart 7). The greatest variations from the standard incidences were found when tenderness was present in the right lower abdominal quadrant with muscular spasm. The remaining groups showed a definite variation from the standard, although not to

TABLE 8.—*Incidence of Inflammatory Change in the Appendix According to a History of Nausea and Vomiting*

	Total Cases	Total without Inflammation	Normal	Atrophic	Total with Inflammation	Simple Chronic Appendicitis	Total with Marked Changes	Chronic Catarrhal Appendicitis	Chronic Exudative Appendicitis	Chronic Obliterative Appendicitis with Infiltration	Chronic Obliterative Appendicitis without Infiltration
Standard*.....	...	41	37	4.3	59	28	31	4.8	8	5.2	10.5
Nausea and vomiting.....	572	29	23	3.7	71	24	47	7.0	26	9.3	4.2
None†.....	298	28	23	4.3	72	26	46	4.7	28	10.6	2.7
Total.....	870	28	24	3.9	72	24	47	6.2	27	9.7	3.7

* The incidence in cases which involve no history or physical findings indicating disease in the appendix is regarded as standard.

† This classification includes all histories in which nausea and vomiting were said not to have occurred or were not mentioned.

TABLE 9.—*Incidence and Follow-Up Cures According to a History of Constipation*

	Total Cases	Incidence, per Cent	Per Cent Cured
Constipation.....	362	42	83
None*.....	519	58	90
Total.....	881	100	87

* This classification includes all histories in which constipation was said not to have occurred or was not mentioned.

such a marked extent. When tenderness was not present in the abdomen, the patient having been operated on because of the history or the findings in previous attacks, the variation from the standard was least after that of the cases in which tenderness was found elsewhere than in the right lower abdominal quadrant. When tenderness was not detected high on the right by rectal or pelvic examination, the variation from the standard was slightly greater than when it was detected. The one exception was in cases of chronic exudative appendicitis, which might well be expected to produce definite tenderness at times.

The percentages of follow-up cures checked very well with the findings just mentioned (table 12, chart 8). The highest incidence (96 per cent) occurred when tenderness was found in the right lower

TABLE 10.—Incidence of Inflammatory Change in the Appendix According to a History of Constipation

	Total Cases	Total without Inflammation	Normal	Atrophic	Total with Inflammation	Simple Chronic Appendicitis	Total with Marked Changes	Chronic Catarrhal Appendicitis	Chronic Exudative Appendicitis	Chronic Obliterative Appendicitis with Infiltration	Chronic Obliterative Appendicitis without Infiltration
Standard*	...	41	37	4.3	59	28	31	4.8	8	5.2	10.5
Constipation.....	358	31	26	4.8	69	23	46	5.6	28	6.2	3.3
None†.....	512	27	23	3.3	73	26	47	6.6	26	10.0	3.9
Total.....	870	28	24	3.9	72	24	47	6.2	27	9.7	3.7

* The incidence in cases which involve no history or physical findings indicating disease in the appendix is regarded as standard.

† This classification includes all histories in which constipation was said not to have occurred or was not mentioned.

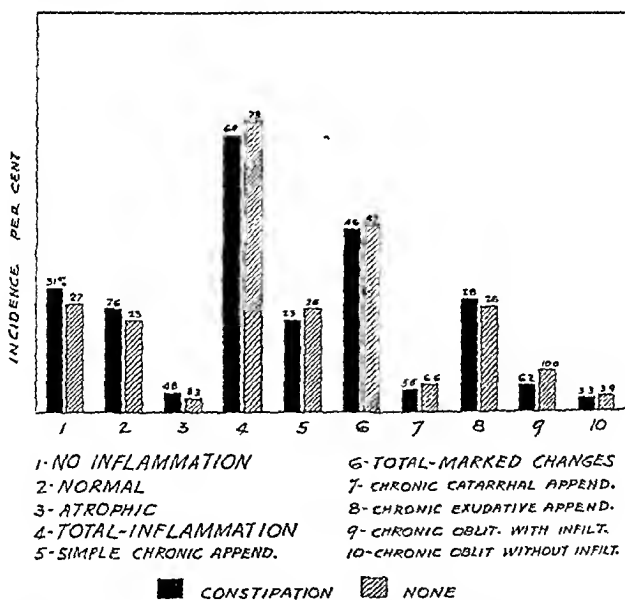


Chart 6.—Incidence of inflammatory changes according to a history of constipation. The incidence is slightly increased in the absence of such a history.

abdominal quadrant associated with muscular spasm. As contrasted to this, when muscular spasm was not present the incidence of cures was 86 per cent, approximately the average for the whole group. No variation was found in the proportion of cures according to whether

tenderness high on the right was or was not detected by rectal or pelvic examination, the figures being 88 and 87 per cent, respectively. The remaining groups were too small to give conclusive figures, but the fact

TABLE 11.—Incidence of Inflammatory Change in the Appendix According to Physical Findings

	Total Cases	Total without Inflammation	Normal	Atrophic	Total with Inflammation	Simple Chronic Appendicitis	Total with Marked Changes	Chronic Catarrhal Appendicitis	Chronic Exudative Appendicitis	Chronic Obliterative Appendicitis with Infiltration	Chronic Obliterative Appendicitis without Infiltration
Standard*.....	41	37	4.3	50	28	31	4.8	8	5.2	10.5	
Tenderness in the right lower abdominal quadrant without muscular spasm.....	578	28	24	3.8	72	26	47	0.4	28	9.0	3.5
Tenderness in the right lower abdominal quadrant with muscular spasm.....	115	23	20	3.5	77	21	56	0.0	34	9.0	5.2
No tenderness in the abdomen.....	145	32	28	3.6	68	28	41	4.1	21	11.7	4.1
Tenderness high on the right detected by rectal or vaginal examination.....	153	30	28	2.6	70	26	44	4.5	30	7.1	2.6
No tenderness detected by rectal or vaginal examination	514	26	22	4.1	74	26	48	7.4	25	11.5	3.7
Tenderness elsewhere	72	42	35	7.0	58	20	38	11.1	15	11.1	0.0
Total.....	870	28	24	3.9	72	24	47	6.2	27	9.7	3.7

* The incidence in cases which involve no history or physical findings indicating disease in the appendix is regarded as standard.

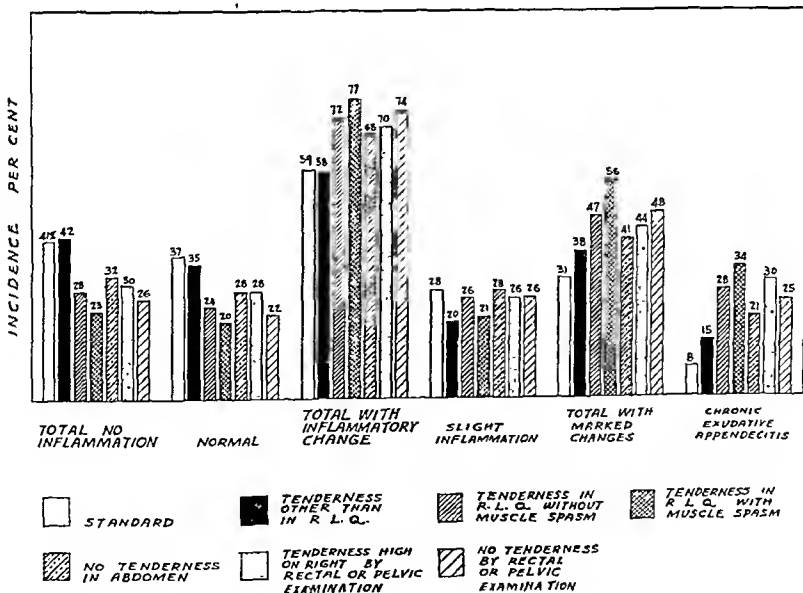
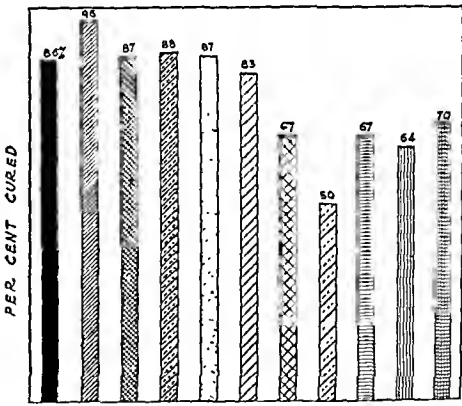
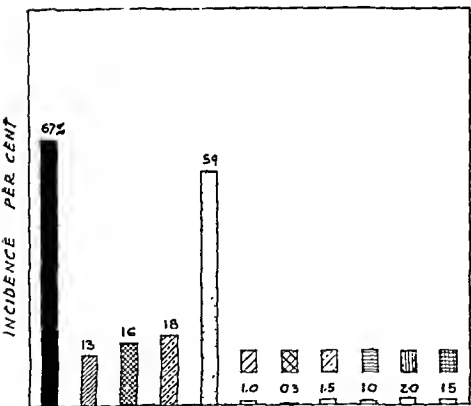


Chart 7.—Incidence of inflammatory changes according to physical findings. Note that the incidences of pathologic changes in cases in which tenderness was found in sites other than the right lower abdominal quadrant approximate very closely those in cases in which the appendixes were removed from patients never suspected of having had appendicitis.

that the incidences were uniformly low and that the total incidences of microscopic pathologic changes checked closely with the incidence found in the absence of symptoms and physical findings (chart 7) would indicate that these figures may be accepted. Physical signs elsewhere than in the right lower abdominal quadrant do not indicate the proba-

TABLE 12.—Incidence and Follow-Up Cures According to Physical Findings

	Total Cases	Incidence, per Cent	Per Cent Cured
Tenderness in the right lower abdominal quadrant or McBurney's point without spasm.....	586	67	86
Tenderness in the right lower abdominal quadrant or McBurney's point with spasm.....	116	13	96
No tenderness in the abdomen.....	147	16	87
Tenderness high on the right detected by rectal or pelvic examination	157	18	83
No tenderness detected by rectal or pelvic examination.....	520	59	87
Tenderness about the umbilicus.....	9	1.0	83
Tenderness in the left lower abdominal quadrant.....	3	0.3	67
Tenderness in the right upper abdominal quadrant.....	16	1.8	50
Tenderness in the entire abdomen	8	0.9	67
Tenderness in the right flank	20	2.3	64
Tenderness in the right costovertebral angle.....	16	1.8	70
Total.....	881	100	87



TENDERNESS R.L.Q. WITHOUT MUSCLE SPASM TENDERNESS R.L.Q. WITH MUSCLE SPASM NO TENDERNESS IN ABDOMEN TENDERNESS HIGH ON RIGHT BY RECTAL OR PELVIC EXAMINATION NO TENDERNESS DETECTED BY RECTAL OR PELVIC EXAMINATION TENDERNESS ABOUT UMBILICUS
TENDERNESS L.L.Q. TENDERNESS R.U.Q. TENDERNESS ENTIRE ABDOMEN TENDERNESS RIGHT FLANK TENDERNESS RIGHT COSTO-VERTEBRAL ANGLE

Chart 8.—Incidence and percentages of cures according to physical findings. The percentages of cures are uniformly low in the cases in which tenderness was present in sites other than the right lower abdominal quadrant. This observation checks with the incidences of inflammatory changes (chart 7).

bility of relief by the removal of the appendix. There is one exception, tenderness in the region of the umbilicus, with 83 per cent follow-up cures; but this site is close to the normal location of the appendix, and tenderness there could very well at times be actual appendical tenderness.

LEUKOCYTE COUNTS

When no leukocyte count was done and when the counts were under 10,000 (table 13), the incidences of the various types of pathologic change found in the appendix presented no appreciable variations from the averages. Associated with counts from 10,000 to 12,000 there was

TABLE 13.—*Incidence of Inflammatory Change in the Appendix According to Leukocyte Count**

	Total Cases	Total without Inflammation	Normal	Atrophic	Total with Inflammation	Simple Chronic Appendicitis	Total with Marked Changes	Chronic Catarrhal Appendicitis	Chronic Exudative Appendicitis	Chronic Obliterative Appendicitis with Infiltration	Chronic Obliterative Appendicitis without Infiltration
Standard†.....	41	37	4.3	59	28	31	4.8	8	5.2	10.5	
No leukocyte count.....	277	30	25	4.7	70	26	44	5.1	24	10.5	4.0
Leukocyte count under 10,000.....	319	28	25	3.4	72	25	47	6.3	28	9.4	3.4
Leukocyte count 10,000 to 12,000.....	116	29	25	4.3	71	19	52	8.6	31	6.9	4.3
Leukocyte count 12,000 to 14,000.....	78	22	21	1.2	78	29	49	9.0	24	14.1	1.2
Leukocyte count 14,000 and over.....	80	29	24	5.0	71	30	41	3.7	25	7.5	5.0
Total.....	870	23	24	3.9	72	24	47	6.2	27	9.7	3.7

* No outstanding trends are in evidence, although there is a tendency to vary from the incidences found in the absence of symptoms as the leukocyte counts increase up to 14,000. When the count is above this figure, the incidences approach nearer to that which occurs when no pathologic condition of the appendix was suspected preoperatively.

† The incidence in cases which involve no history or physical findings indicating disease in the appendix is regarded as standard.

TABLE 14.—*Incidence and Follow-Up Cures According to Leukocyte Count**

Leukocyte count	Total Cases	Incidence, per Cent†	Per Cent Cured				Entire Group
			Inflammation in Appendix			Total	
			None	Slight	Marked		
Under 10,000.....	320	54	82	94	90	91	90
10,000 to 12,000.....	117	19	82	94	92	92	90
12,000 to 14,000.....	78	13	83	90	90	90	89
14,000 and over.....	82	14	83	81	96	90	88
Total.....	597	100‡	82	91	91	91	89

* No relation between the leukocyte counts and follow-up cures can be demonstrated.

† Percentages are based on 597 cases in which leukocyte counts were done.

‡ Of all the cases studied, leukocyte counts were recorded in 68 per cent.

little change from the averages, although a slight increase in the incidences of inflammatory changes was present. This became somewhat more noticeable when the counts were from 12,000 to 14,000. When they were above the latter figure the percentages dropped back to or below the averages. The percentages of follow-up cures held close to the averages throughout (table 14), notwithstanding differences in the leukocyte counts.

PREOPERATIVE DIAGNOSES

The preoperative diagnosis is the surgeon's total impression of the history, the physical examination and the reports from the laboratory. Here it may be considered as a measure of the severity of the symptoms,

TABLE 15.—Incidence of Inflammatory Change in the Appendix According to Preoperative Diagnosis

	Total Cases	Total without Inflammation	Normal	Atrophic	Total with Inflammation	Simple Chronic Appendicitis	Total with Marked Changes	Chronic Catarrhal Appendicitis	Chronic Exudative Appendicitis	Chronic Obliterative Appendicitis with Infiltration	Chronic Obliterative Appendicitis without Infiltration
Standard*.....	41	37	4.3	59	28	31	4.8	2	5.2	10.5	
Diagnosis of chronic appendicitis.....	308	33	27	6.5	67	25	42	5.5	23	8.4	4.9
Diagnosis of interval appendectomy.....	188	31	28	3.2	69	30	38	6.4	17	9.6	5.3
Diagnosis of subacute appendicitis.....	233	25	23	2.6	75	21	54	6.9	36	9.5	0.9
Diagnosis of acute appendicitis.....	116	20	18	1.7	80	24	56	6.0	34	12.1	4.3
Other diagnoses.....	25	16	16	0.0	84	24	60	8.0	36	16.0	0.0
Total.....	870	28	24	3.9	72	24	47	6.2	27	9.7	3.7

* The incidence in cases which involve no history or physical findings indicating disease in the appendix is regarded as standard.

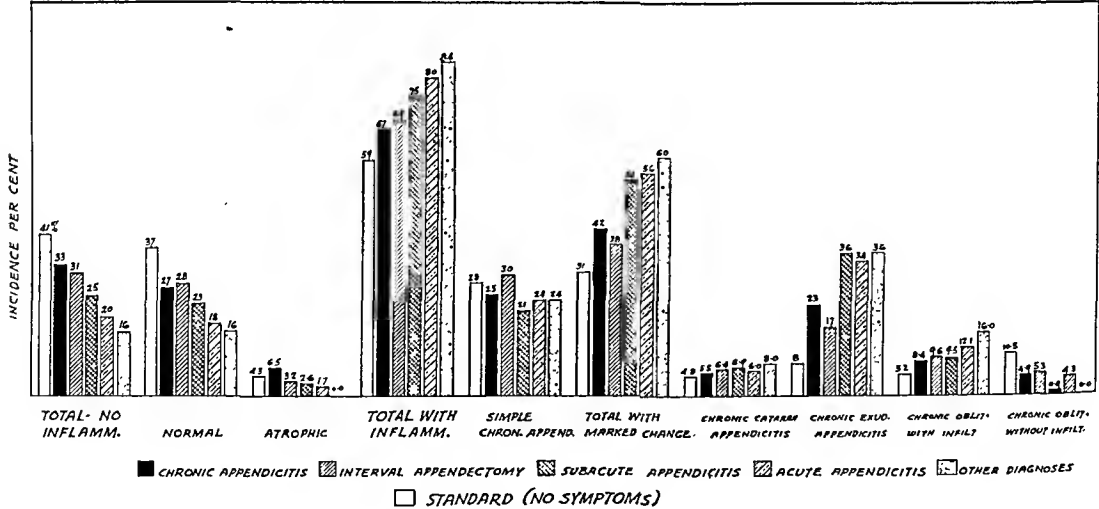


Chart 9.—Incidence of inflammatory changes according to the preoperative diagnosis. The chart demonstrates the fact that the more severe the symptoms and physical findings (as indicated by the preoperative diagnoses), the more the incidences of inflammatory changes vary from those found in cases in which the patients had had no symptoms or physical findings attributed to the appendix. An exception is found in the cases in which other diagnoses than appendicitis were made, but these were cases of patients in the older age groups.

the seriousness of the physical findings and the increase in the leukocyte count, provided the last group, "other diagnoses" (table 15), is temporarily ignored. The incidences of inflammatory changes varied directly, and noticeably, with the severity of the symptoms, etc., as indicated by the preoperative diagnoses (table 15, chart 9). The total incidence of inflammatory changes, the total incidence of marked changes, the incidence of chronic exudative appendicitis and the inci-

TABLE 16.—Incidence and Follow-Up Cures According to Preoperative Diagnosis

Diagnosis of	Total Cases	Incidence, per Cent	Per Cent Cured				Entire Group
			Inflammation in Appendix				
			None	Slight	Marked	Total	
Chronic appendicitis.....	309	25	79	91	81	85	82
Interval appendectomy.....	191	22	84	84	93	89	88
Subacute appendicitis.....	237	27	80	97	95	96	92
Acute appendicitis.....	119	13	89	91	94	93	91
Other diagnoses.....	23	3	86	75	67	69	74
Total.....	881	100	80	90	89	90	87

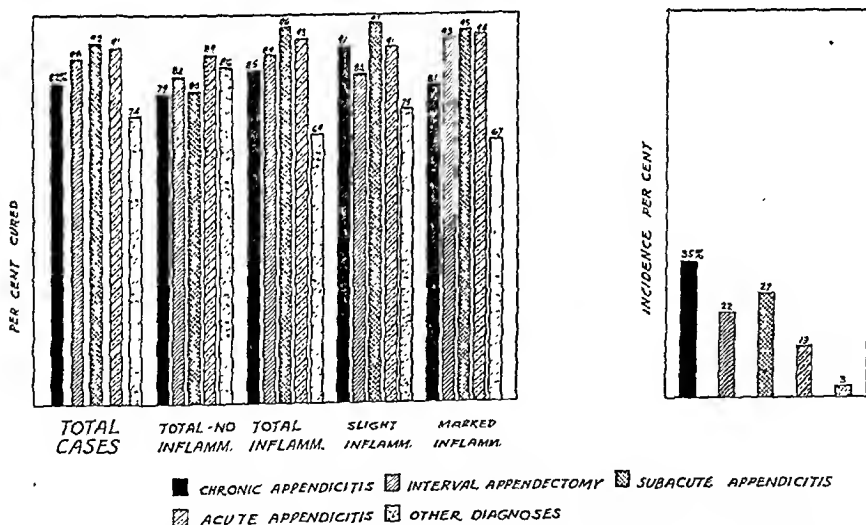


Chart 10.—Percentages of cures and incidence according to the preoperative diagnosis. Throughout, the best percentages of follow-up cures were attained when the diagnosis was subacute or acute appendicitis, and the poorest when some preoperative diagnosis other than appendicitis had been made.

dence of chronic obliterative appendicitis with infiltration increased with the severity of the symptoms as indicated by diagnoses. Incidence in the other groups showed no definite variations in either direction.

In the group of cases classified under the heading "other diagnoses," the number of appendixes studied was too small for the figures to be conclusive. The high incidence of inflammatory changes was due to

the fact that the average age of the patients was past middle life. The effect of age on these incidences will be taken up later in this paper. The distribution of the low percentages of follow-up cures was as uniform as could be expected in view of the small number of cases in this group, 25 (table 16, chart 10). The average, 74 per cent, was by far the lowest proportion of cures found in the various groups as classified according to preoperative diagnoses. This circumstance checked very well with the fact that correspondingly low percentages of follow-up cures resulted when tenderness was found elsewhere than in the right lower quadrant (chart 8). The proportion of cures in the cases in which the diagnosis was chronic appendicitis was somewhat below the average, 82 per cent; in the cases in which the diagnosis indicated interval appendectomy, it was about the average, 88 per cent, and in the cases in which the diagnosis was subacute or acute appendicitis, it was high, 92 and 91 per cent, respectively. The particularly interesting point is that these figures checked with the incidences of inflammatory changes.

TABLE 17.—*Incidence and Follow-Up Cures According to the Wassermann Reaction**

	Total Cases	Incidence, per Cent	Per Cent Cured
Negative reaction.....	643	98	88
Positive reaction.....	16	2.4	100
Total.....	659†	100	88

* This table is of interest only in that it shows the incidence of positive Wassermann reactions in the series. No evidence of syphilis was found by microscopic examination of the appendixes.

† Wassermann tests were done in 75 per cent of the 881 cases studied.

WASSERMANN REACTIONS

Wassermann reactions were reported in 659 cases, 75 per cent of the total studied. Of these, 16 reactions were positive (table 17), giving an incidence of 2.4 per cent. It is interesting to note that in this small group no patients returned with a recurrence of symptoms. Sections of the appendixes from all of the patients with positive Wassermann reactions were reviewed, and in none could any evidence of syphilitic lesions be found.

SEX

A slight but uniform increase in the incidences of inflammatory changes was found in the appendixes removed from men as compared with those from women (table 18, chart 11 A). This information checked with the fact that there was a somewhat higher percentage of follow-up cures in the cases of men, 90 per cent as compared to 86 per cent (table 19, chart 11 B). The total number of patients was made up one third of men and two thirds of women.

AGE

The percentages of follow-up cures showed no great variations with increase in the age of the patients (table 20, chart 12). It is of interest,

TABLE 18.—Incidence of Inflammatory Change in the Appendix According to Sex

	Total Cases	Total without Inflammation	Normal	Atrophic	Total with Inflammation	Simple Chronic Appendicitis	Total with Marked Changes	Chronic Catarrhal Appendicitis	Chronic Exudative Appendicitis	Chronic Obliterative Appendicitis with Infiltration	Chronic Obliterative Appendicitis without Infiltration
Standard*.....	...	41	37	4.3	50	28	31	4.8	8	5.2	10.5
Male.....	285	27	22	5.3	73	23	49	6.6	29	9.8	3.5
Female.....	585	29	26	3.2	71	26	45	6.0	23	9.6	3.8
Total.....	870	28	24	3.9	72	24	47	6.2	27	9.7	3.7

* The incidence in cases which involve no history or physical findings indicating disease in the appendix is regarded as standard.

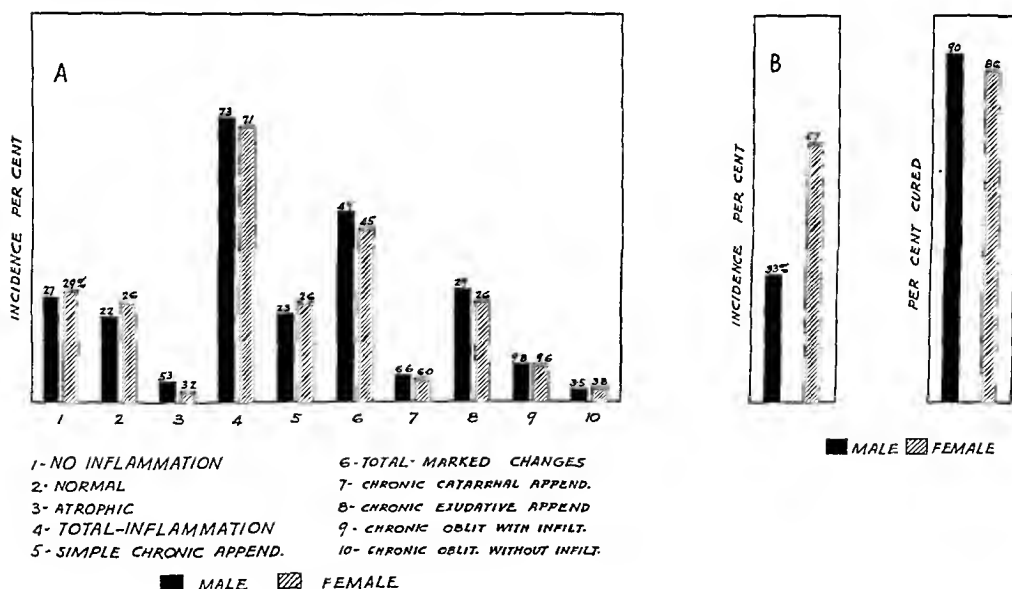


Chart 11.—A, incidence of inflammatory changes according to sex. The incidence is slightly higher in the appendixes removed from men. B, incidence and percentages of cures according to sex. Corresponding to the increased incidence of inflammatory changes in the appendixes removed from men there is a slight increase in the follow-up cures.

however, to note that the two lowest figures were for the age groups 41 to 50 and 21 to 30 (80 and 84 per cent, respectively). These ages coincide with two periods of physical and mental change in women; i. e.,

the menopause and the period of adjustment to sex and to family or business life. The incidences of inflammatory changes in the appendixes varied with increase in the patients' ages (table 21, chart 13) much as did those in the appendixes which had not been the cause of symptoms or physical findings, but the variations were more marked.

TABLE 19.—Incidence and Follow-Up Cures According to Sex

	Total Cases	Incidence, per Cent	Per Cent Cured
Male.....	289	33	90
Female.....	502	67	86
Total.....	881	100	87

TABLE 20.—Incidence and Follow-Up Cures According to Age

	Total Cases	Incidence, per Cent	Per Cent Cured
Age 1 to 10.....	25	3	94
11 to 20.....	351	40	89
21 to 30.....	320	36	84
31 to 40.....	126	14	88
41 to 50.....	41	5	80
51 to 60.....	18	2	86
Total.....	881	100	87

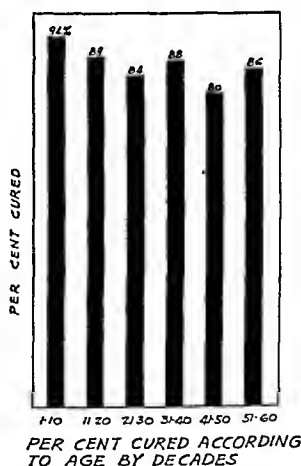
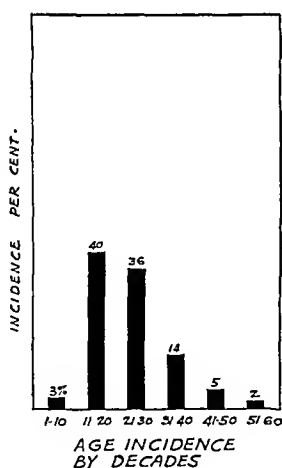


Chart 12.—Incidence and percentages of cures according to age. Seventy-six per cent of the patients were between the ages of 11 and 30. The lowest percentage of follow-up cures is found in the years of the menopause in women. This observation would indicate that in this period of life accurate diagnosis is most difficult.

With increase in the age of the patients, the following changes in incidences appeared: a marked decrease in the incidence of normal appendixes and, in the presence of symptoms, of chronic exudative

TABLE 21.—Incidence of Inflammatory Change in the Appendix According to Age*

Standard†	Total Cases	Total without Inflammation	Normal	Atrophic	Total with Inflammation	Simple Chronic Appendicitis	Total with Marked Changes	Chronic Catarrhal Appendicitis	Chronic Exudative Appendicitis	Chronic Obliterative Appendicitis with Infiltration	Chronic Obliterative Appendicitis without Infiltration
Age 1 to 10.....	24	33	33	0.0	67	21	46	8.3	38	0.0	0.0
11 to 20.....	349	34	30	3.7	66	25	42	4.9	28	6.9	1.5
21 to 30.....	315	30	26	3.8	70	24	46	5.7	26	10.8	3.2
31 to 40.....	125	17	12	5.0	83	24	59	8.0	23	13.6	8.9
41 to 50.....	40	15	8	7.4	85	27	58	10.0	20	17.5	10.0
51 to 60.....	17	6	6	0.0	94	29	65	17.7	24	11.8	11.8
Total.....	870	28	24	3.9	72	24	47	6.2	27	9.7	3.7

* The trends indicated in this table are much better shown in chart 13.
† The incidence in cases which involve no history or physical findings indicating disease in the appendix is regarded as standard.

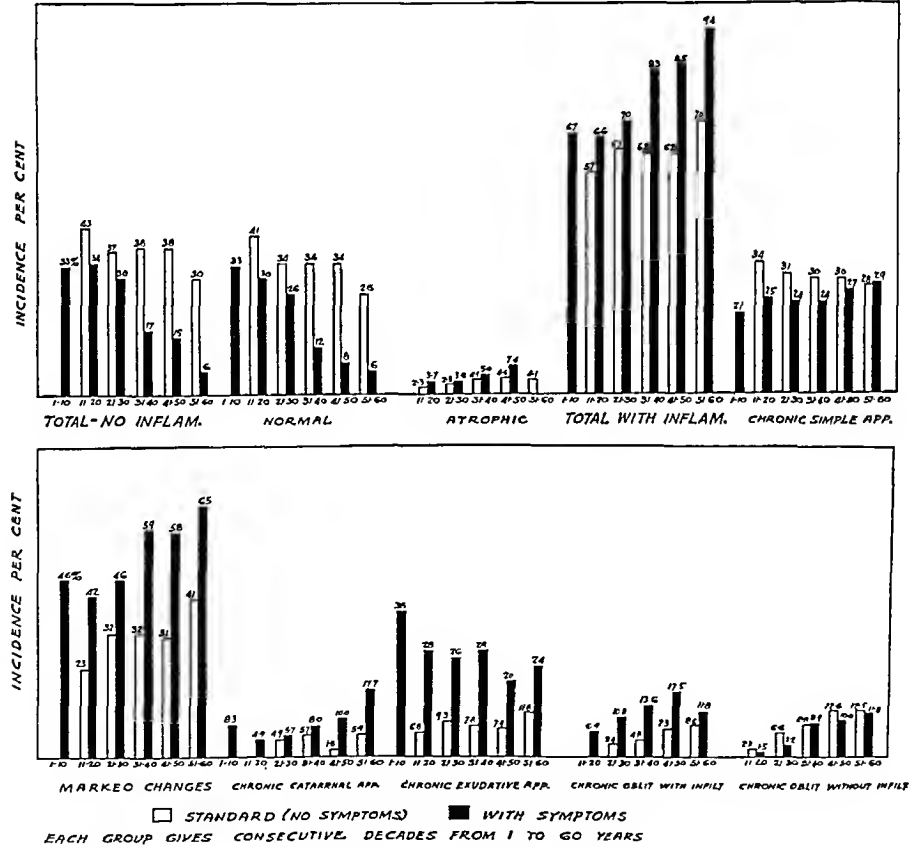


Chart 13.—Incidence of inflammatory changes according to age in the presence and in the absence of symptoms. This chart demonstrates the marked accentuation of the effect of age on the inflammatory changes in the appendix when symptoms are present. This statement does not hold true of simple chronic appendicitis, perhaps because the recurring attacks cause more advanced pathologic changes to appear.

appendicitis, though the latter in the absence of symptoms showed no definite trend; a marked increase in the incidence of atrophic appendixes, chronic catarrhal appendicitis and chronic obliterative appendicitis with and without infiltration, and no marked change in simple chronic appendicitis, although a slight increase was found in the presence of symptoms, whereas a slight decrease occurred in the absence of symptoms. Subacute appendicitis, which pathologically closely approximates chronic exudative appendicitis, also decreases in incidence with increase in the age of the patients.

PATHOLOGIC CONDITIONS OTHER THAN NONSPECIFIC INFLAMMATION

Adhesions and Fecaliths.—A detailed discussion of adhesions and fecaliths was given in connection with tables 3 and 4. Since their incidences were not noted in the absence of symptoms and physical findings attributable to the appendix, no comparisons can be made.

Foreign Body in the Lumen of the Appendix.—Foreign bodies were found 12 times, an incidence of 1.4 per cent, as compared with 0.2 per cent in the absence of symptoms and physical findings.

Oxyuris was noted in 10 appendixes, an incidence of 1.1 per cent, as compared with 0.2 per cent when a pathologic condition of the appendix was not suspected preoperatively. The microscopic examination showed a normal appendix in 1 case, simple chronic appendicitis in 3 and chronic exudative appendicitis in 6. Adhesions were present in 3 cases and fecaliths in 2. The appendix was removed in the first attack in 7 cases, while in the remaining 3 intermittent attacks had occurred for from three to six months. All of the patients presented tenderness at McBurney's point, but only 2 had definite muscular spasm. The total leukocyte counts varied between 7,300 and 22,500 and the differential counts from 74 per cent polymorphonuclears and 26 per cent lymphocytes to 88 per cent polymorphonuclears and 12 per cent lymphocytes. No eosinophils were found in any of the 10. Eight patients were followed, and none had a return of the preoperative symptoms.

A small piece of wire was found in 1 appendix. Microscopically, the pathologic condition was chronic exudative appendicitis. The patient had had continuous pain in the right lower abdominal quadrant for the three months preceding the operation. Tenderness was present at McBurney's point without muscular spasm. The total leukocyte count was 9,000, with 62 per cent polymorphonuclears, 26 per cent lymphocytes, 10 per cent eosinophils and 2 per cent basophils. There were no adhesions about the appendix, but it contained a fecalith. This patient was the only one in the series presenting definite eosinophilia. She had no return of the preoperative symptoms.

A seed was present in one appendix. The patient had had three attacks of pain in the right lower abdominal quadrant in the five months preceding the operation. Tenderness was present at McBurney's point

TABLE 22.—Incidence and Follow-Up Cures According to Pathologic Condition Other than Nonspecific Inflammation

	Total Appendixes	Incidence, per Cent*	Standard Incidence†	Per Cent Cured‡
Adhesions§.....	430	48	...	89
Fecaliths§.....	156	18	...	89
Foreign body in the lumen.....	12	1.4	0.2	100
Oxyuris.....	10	1.1	0.2	100
Wire.....	1	0.1	0.0	100
Seed.....	1	0.1	0.0	100
Mucocele.....	2	0.2	0.2	100
Diverticulum.....	2	0.2	0.1	100
Lymphoid hyperplasia.....	1	0.1	0.0	...
Tuberculosis.....	2	0.2	0.3	100
Tumors.....	7	0.8	0.3	100
Carcinoid.....	6	0.7	0.1	100
Carcinoma.....	1	0.1	0.1	100
Total.....	612	60	1.5	89

* Percentages are based on the 881 cases studied.

† The incidence in cases which involved no history or physical findings indicating disease in the appendix is regarded as standard.

‡ The percentages of follow-up cures hold uniformly high in the presence of these various pathologic conditions.

§ Both adhesions and fecaliths were present in 99 cases.

|| No follow-up was made in this case.

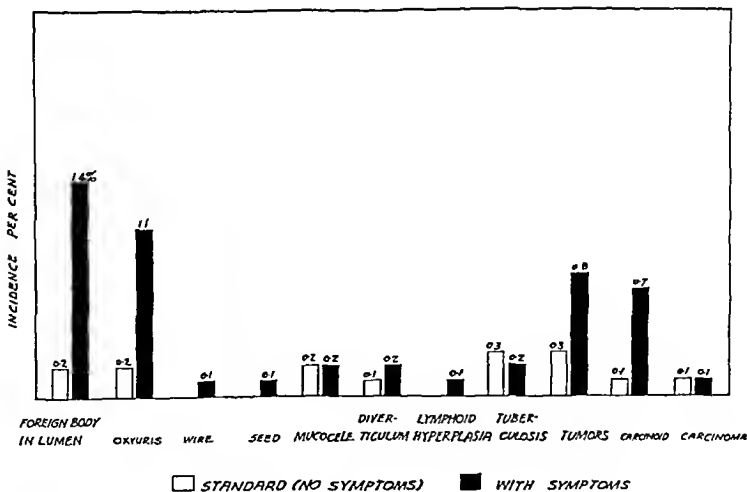


Chart 14.—Comparison of the incidence of pathologic conditions other than nonspecific inflammatory changes in the presence and in the absence of symptoms. With foreign bodies in the lumen of the appendix and with tumors, the incidences are markedly increased in the presence of symptoms referable to the appendix.

with muscular spasm. Adhesions were found about the appendix. Microscopic examination showed only simple chronic appendicitis. This patient had no postoperative return of symptoms.

Mucocoele of the Appendix.—Mucocoele was found twice, an incidence of 0.2 per cent, which is the same as that found when no symptoms or physical findings indicated a pathologic process in the appendix. One of the patients had had recurrent attacks of pain in the right side of the abdomen for ten years; the other was operated on in the first attack. One presented a normal abdomen; the other, tenderness at McBurney's point without muscular spasm. A leukocyte count done on 1 gave the following results: The total count was 10,000, with 66 per cent polymorphonuclears and 34 per cent lymphocytes. Both patients were followed, and neither had a recurrence of symptoms.

Diverticulum of the Appendix.—Two appendixes showed diverticula, an incidence of 0.2 per cent, as compared with 0.1 per cent when no symptoms were noted. Both patients had had recurrent attacks of pain in the right lower abdominal quadrant, 1 for five months and the other for eighteen months. Both had tenderness at McBurney's point without muscular spasm. No leukocyte counts were made. In each case the uninvolved part of the appendix showed chronic exudative inflammation. Both patients were followed, and no recurrence of symptoms occurred.

Lymphoid Hyperplasia.—Only 1 case of lymphoid hyperplasia was found, an incidence of 0.1 per cent. The patient had had recurrent attacks of pain in the right lower abdominal quadrant for one year. Tenderness was present at McBurney's point without muscular spasm. No adhesions were present. The patient did not return to the follow-up clinic.

Tuberculosis of the Appendix.—Two appendixes were tuberculous, an incidence of 0.2 per cent, as compared with 0.3 per cent when no symptoms or physical findings referable to the appendix were noted. The higher percentage in the latter group may be due to the fact that among the tuberculous appendixes removed at incidental appendectomies were several removed at operations for some other tuberculous condition in the abdomen. One of the patients was operated on in the first attack, the other having had recurrent attacks for three months. Tenderness was present at McBurney's point with muscular spasm in both cases. The leukocyte count of the patient in the first attack was 19,300, with 88 per cent polymorphonuclears and 12 per cent lymphocytes; that of the patient with recurrent attacks was 8,100, with 68 per cent polymorphonuclears and 32 per cent lymphocytes. Pathologically, both appendixes showed chronic tuberculous appendicitis. Neither patient had any return of the abdominal symptoms, although both had continued activity of the pulmonary lesions.

Tumor of the Appendix.—Tumor was found in 7 appendixes, an incidence of 0.8 per cent, as compared with 0.3 per cent in the absence of symptoms or physical findings pointing to a pathologic condition in the appendix.

A carcinoid of the appendix was noted 6 times. Two of the patients were operated on in their first attacks of pain in the right lower abdominal quadrant, the others having had recurrent attacks, 3 for one year or less and the other for many years. The leukocyte counts varied from 7,000 to 18,000 and the differential counts from 76 per cent polymorphonuclears and 24 per cent lymphocytes to 82 per cent polymorphonuclears and 18 per cent lymphocytes. Two patients had normal abdomens, while 4 had tenderness at McBurney's point, of whom 2 had definite muscular spasm. The entire appendix was involved in 1 case. Microscopic examination in the others showed, in the remainder of the appendix, normal conditions in 2 cases, simple chronic appendicitis in 1, chronic obliterative appendicitis in 1 and adhesions in 1. Five patients were followed, of whom none had any return of the symptoms.

TABLE 23.—*Postoperative Deaths**

Cause of Death	Time Postoperative
Respiratory failure, pulmonary edema.....	30 minutes
Peritonitis due to <i>Streptococcus haemolyticus</i>	7 days
Pulmonary embolus	11 days
Acute infection of the upper part of the respiratory tract, purpura haemorrhagica, acute pericarditis, chronic fibrous pleuritis.....	62 days

* The total number of deaths was 4, a mortality of 0.45 per cent.

† The incidence of peritonitis for the 881 operations was 0.1 per cent.

A carcinoma of the appendix (infiltrating type) was found in 1 case. The appendix contained a fecalith, but there were no adhesions about it. The patient had had recurrent attacks of pain in the right lower abdominal quadrant for two and one-half years, the last having occurred six weeks before the operation. The abdomen was normal on physical examination. After the operation there was no return of the preoperative symptoms and no evidence of recurrence of the malignant growth up to the time when the patient was last seen, more than one year later.

POSTOPERATIVE DEATHS

Four deaths occurred postoperatively in the 881 cases, a mortality of 0.45 per cent. One patient died thirty minutes after operation of respiratory failure. Autopsy revealed only pulmonary edema. This patient had had recurrent attacks of pain in the right lower abdominal quadrant for two years, four in the two weeks before admission. At the time of entrance to the hospital the leukocyte count was 12,000, with 78 per cent polymorphonuclears, 20 per cent lymphocytes and

2 per cent eosinophils. Three days later the count was 8,000, with 76 per cent polymorphonuclears and 24 per cent lymphocytes. The operation was done two days after that. The appendix was bound down and kinked in the middle by adhesions. Microscopically, it showed chronic obliterative appendicitis.

A second patient died seven days after operation of peritonitis due to *Streptococcus haemolyticus*. At autopsy the region of the cecum was found to be normal. This patient had had two attacks of pain in the right lower abdominal quadrant, the first a year and the second six weeks before the operation. The appendix was found kinked in the middle by adhesions and was microscopically normal.

Two other patients died after leaving the surgical service. One died of pulmonary embolus on the eleventh day after operation, two days after leaving the hospital. This patient had had recurrent attacks of pain in the right lower abdominal quadrant for six years, the last occurring ten days before admission. The leukocyte count was 10,500, with 78 per cent polymorphonuclears and 22 per cent lymphocytes. The appendix was kinked by adhesions and microscopically showed chronic obliterative appendicitis with infiltration.

The last fatality was in the case of a patient who died two months after operation, while under treatment in the medical service. Up to the eleventh day after operation her convalescence was uneventful. An acute sore throat then developed, with infection in the ethmoid sinuses and antrums. The diagnosis during the illness, confirmed at autopsy, was purpura haemorrhagica, acute pericarditis and chronic fibrous pleuritis. On admission the patient had given a history of attacks of pain in the right lower abdominal quadrant for six months, the last having been present at the time of admission. Examination of the abdomen showed tenderness at McBurney's point without muscular spasm. The leukocyte count was 10,000, with 80 per cent polymorphonuclears and 20 per cent lymphocytes. The appendix was bound down by adhesions and appeared edematous. Microscopically, it showed a marked chronic exudative appendicitis. During the two months of her postoperative illness the patient had no attacks of pain in the right lower abdominal quadrant. It might well be considered that this last case should not be included in the calculation of postoperative mortality.

SUMMARY

A critical study has been made of 881 cases in which appendectomy was performed because of symptoms attributed, either before or after the operation, to a nonspecific chronic inflammation in the appendix. The microscopic observations in these appendixes were compared with a standard, the incidences of microscopic pathologic conditions when

there were no symptoms or physical findings attributable to the appendix and no inflammation noted elsewhere in the abdomen. A considerable increase in inflammatory changes was found, due entirely to the marked increase in the incidences of chronic exudative appendicitis and chronic obliterative appendicitis with infiltration. A corresponding decrease in the incidence of normal appendixes occurred.

The percentages of follow-up cures were found to be low when no inflammatory changes were present, cases involving atrophic appendixes giving the lowest figure. When inflammatory changes were found, a higher percentage of follow-up cures resulted from appendectomy. These cures appeared not to depend on the type of inflammatory change present or its variation from the standard incidence as described. When adhesions or fecaliths were found with a normal appendix, the percentage of follow-up cures was increased almost to those found when inflammatory changes were present in the appendix.

When the patients gave a history of more than one attack occurring within a period of one year or less, the percentage of follow-up cures was remarkably high. It was low when the attacks covered a period longer than one year and was still lower when the patients were operated on during or following the first attack. The incidences of inflammatory changes were unaffected by the presence or absence of a history of nausea and vomiting, although the percentage of follow-up cures was slightly decreased in the presence of such a history. When a history of constipation was given, the incidences of inflammatory changes decreased slightly, as did the percentage of follow-up cures.

Both the incidences of inflammatory changes and the percentages of follow-up cures varied directly with the definiteness of localization and the seriousness of the physical findings in the right lower abdominal quadrant, the highest figures being obtained when both tenderness and muscular spasm were present. When tenderness was found elsewhere in the abdomen than in the right lower quadrant, the incidences of inflammatory changes checked almost exactly with those for the patients who had had no symptoms or physical findings referable to the appendix and the lowest percentages of follow-up cures resulted. When the patients were operated on only because of the history of attacks of pain in the right lower abdominal quadrant, no tenderness having been found after admission to the hospital, the results were the same as the average for the whole group studied. The presence or absence of tenderness high on the right detected by rectal or vaginal examination bore no apparent relation to the incidences of inflammatory changes or to the percentages of follow-up cures.

The leukocyte counts did not appear to bear a definite relation to the follow-up cures or to the incidences of pathologic change, although with a moderate increase in the leukocyte counts there was a slight

increase in the incidences of inflammatory changes. The incidences of inflammatory changes in the appendix were found to vary directly with the definiteness of the localization and the severity of the patient's symptoms as indicated by the diagnoses. This relation was corroborated by an equivalent increase in the follow-up cures in the same sequence. When diagnoses other than appendicitis were made preoperatively and the symptoms attributed to the appendix after operation, the percentage of follow-up cures was low notwithstanding a high incidence of inflammatory changes. (The average age of these patients was much higher than that in the other groups.) This finding checked with the equally low percentages of follow-up cures when tenderness had been noted elsewhere in the abdomen than in the right lower quadrant.

The incidence of positive Wassermann reactions was 2.4 per cent. This condition bore no demonstrable relation to either the pathologic condition of the appendix or the follow-up cures. The ratio of men to women was 1:2, with a slight increase in the incidences of inflammatory changes and percentage of follow-up cures in the men. With an increase in the age of the patients there was a marked increase in the incidences of atrophic appendixes, chronic catarrhal appendicitis and chronic obliterative appendicitis with and without infiltration; no definite change occurred in the incidences of simple chronic appendicitis and chronic exudative appendicitis, and a marked decrease took place in the incidences of normal appendixes. The changes with increase in the age of the patients were much greater than in the appendixes from patients who had not been suspected preoperatively of ever having had any appendical pathologic condition. Even after the small number of appendixes presenting pathologic changes other than inflammatory changes was taken into account, the figures did show that these conditions increased in incidence in the presence of symptoms and physical findings attributed to the appendix and that appendectomy did give relief from those symptoms.

CONCLUSIONS

1. A chronic inflammatory process, adhesions, fecaliths or combinations of these conditions in the appendix have been shown to be the cause of definite symptoms and physical findings which can be relieved by appendectomy. A general term "chronic appendicitis" is suggested to cover these conditions.

2. In properly selected cases, an appendectomy for chronic appendicitis gives an excellent expectation of cure, but the following points should be borne in mind: (a) In the presence of a history of nausea and vomiting or of constipation, especially in women, particular care must be exercised in the selection of cases. (b) The more definite and

localized the physical findings, the better is the expectation of cure. When tenderness is found in other parts of the abdomen than the right lower quadrant, one should be most reluctant to attribute the patient's symptoms to chronic appendicitis. (*d*) The expectation of cure is excellent when the history is of more than one attack within a period of one year or less, much poorer when the attacks cover a period longer than one year and poorest when the patient is operated on in or following the first attack.

3. When no inflammatory change is found in the appendix, the expectation of cure is not good unless either adhesions or fecaliths are present, in which case the results are nearly equal to those obtained when inflammatory changes are present.

4. Owing to recurrent attacks, there is evidently an increase in the pathologic condition in the appendix, as the change with age is much more marked than in the absence of symptoms attributable to the appendix.

5. A mortality of less than 0.5 per cent in the 881 appendectomies would indicate that the operation for the cure of chronic appendicitis is a safe procedure.

6. Incidentally, it has been shown that when a patient has been operated on because of symptoms and physical findings diagnostic of acute or subacute appendicitis and, instead, one of the types of chronic appendicitis (or adhesions or fecaliths without inflammation) is found, the expectation of a permanent cure is excellent. Ordinarily the surgeon lists these as mistaken diagnoses, but the figures as to the marked increase of the incidences of inflammatory changes above those when no symptoms had been attributed to the appendix and the high percentages of follow-up cures found in this study would indicate that the surgeon under such circumstances has benefited the patient almost as much as though acute appendicitis had been found.

One must bear in mind that before operating on any patient for chronic appendicitis because of the conclusions arrived at in this paper, the utmost in diagnostic acumen must be exercised in ruling out all conditions which give a picture simulating that presented by chronic appendicitis. The question of differential diagnosis was outside the limitations of this paper and can be considered only after one has established the fact that there is definitely such a clinical entity as chronic appendicitis.

The pathologic examinations of all the appendixes in this and the preceding study were made by Dr. Leila C. Knox.

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SUBACUTE INFECTIONS OF BONE

OSTEOPERIOSTITIS ALBUMINOSA OLLIER

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Some years ago there came under my observation a case of superficial osseous destruction—osteoperiostitis—showing peculiar clinical and anatomic characteristics as well as diagnostic difficulties (case 1). During the winter of 1935 a second case presented itself, with a strikingly similar history, clinical course, roentgenographic appearance and pathologic condition (case 2). These were obviously cases of bony infection by attenuated organisms of low virulence (staphylococci). The infection was indolent from its beginning and at no time caused the usual local or general acute symptoms. It was in many ways different from other acute and subacute forms of osseous infection, especially from those described by Brodie and Garré. Since these 2 cases were observed, 2 others with similar characteristics have presented themselves.

The condition corresponds to that described in medical literature as "osteoperiostitis albuminosa." It is not mentioned in the usual standard works on surgery or pathology, and reference is made to it only occasionally in the general American literature. Even then it is chiefly noticed in connection with the etiology of bony cysts. For years it has claimed the lively interest of French and German observers. Ollier was the first to note the condition (1864), and at his behest a second case was reported by his pupil Poncet¹ in 1874. Since that time accounts of new cases have slowly trickled into the general literature, so that the reported cases now number around 66. The first report of an American case was made by Dupuis² in 1889. The only other cases reported in the American literature are those reviewed by Pickrell and Schmidt³ in 1910 and Hartwell⁴ in 1911. Most writers, even the most recent, have stressed the rarity of the condition. During the past seventy years the clinical picture of the disease has come to be well defined in

1. Poncet, M. A.: *De la périostite albumineuse*, *Gaz. hebd. de méd.* **11**:133 (Feb.); 179 (March) 1874.

2. Dupuis, T. R.: *A Case of Periostitis Albuminosa of Ollier*, *Canada Lancet* **21**:357 (Aug.) 1889.

3. Pickrell, G., and Schmidt, L. M.: *Chronic Nonsuppurative Osteoplastic Periostitis of Traumatic Origin*, *U. S. Nav. M. Bull.* **4**:1 (Jan.) 1910.

4. Hartwell, J. A.: *Periostitis Albuminosa*, *Proc. New York Path. Soc.* **10**: 55, 1910-1911.

all its phases. It is essentially that of a localized, indolent swelling consisting of periosteal, subperiosteal, parosteal or intermuscular accumulations of clear, serous, stringy or mucoid exudate. This exudate often resembles the white of an egg or synovial fluid.⁵ It has a high albumin content, is frequently encapsulated and on culture may show the presence of ordinary pus organisms (staphylococci). The usual symptoms of infection are absent. An analogue is a form of osseous cyst showing similar characteristics which because of its benign course may develop over years.

REVIEW OF THE LITERATURE ⁶

In reviewing the available literature, I was able to trace 66 cases reported between 1864 and 1934. While this review was in preparation, allusion was made in the more recent literature to 4 or 5 other cases, but these have not been available for inclusion. In the reports of some cases many data of importance are missing, but most of them are fairly complete in essentials.

Incidence.—Of the reported cases in which sex was indicated, 51 were those of men or boys and 10 of women or girls. In 4 cases the age was given as "young"; in 2 it was not mentioned. Eight patients were in the first decade of life, 26 in the second, 12 in the third, 9 in the fourth, 6 in the fifth, 3 in the sixth and 1 (a woman aged 79) in the eighth. The femur was involved in 33 cases (the distal end in 19, the middle third in 8 and the proximal end in 6), the tibia in 21 (the distal end in 8, the middle third in 2 and the proximal end in 9), the humerus in 5 (the distal end in 2 and the proximal end in 2), the ulna in 4 (the distal end in 1, the middle third in 1 and the proximal end in 2), the radius in 1, the phalanges of the fingers in 2, the ilium in 4, a rib in 1 and the skull in 1. There were 4 cases in each of which two bones were involved: femur and rib, femur and humerus, tibia and ulna, and tibia and humerus.

Duration.—The duration of symptoms previous to the time of observation was noted as follows: from four days to one month in 12 cases, from one to two months in 9, from three months to one year in 13, from one to two years in 10, five years in 1 and from ten to twenty-nine years in 6.

5. Poncet (1874): "Une forme spéciale de périostite non décrite jusqu'ici, caractérisée anatomiquement par l'accumulation sous le périoste et dans les couches périostales d'un liquide visqueux, analogue à la synovie. . . . Ajoutons la présence fréquente pour certaines formes de gouttelettes de graisse en plus ou moins grande abondance, rappelant le bouillon gras. . . . le liquide n'est pas toujours visqueux, analogue à du blanc d'œuf. M. Ollier a trouvé une fois entre autres au fémur un liquide séreux, non filant mais clair, avec quelques gouttelettes huileuses."

6. Miss Gladys Ramsey, librarian at the University of Wisconsin, aided in collecting for study the widely scattered sources.

The Exudate.—The disease was identified in the reported cases only after aspiration or incision. In 32 cases the fluid removed was described as serous and stringy (yellow, clear yellow, serous and purulent in 1 each), in 11 as jelly-like, in 17 as serosanguineous (resembling jelly in 5 and purulent in 1), in 1 as resembling glycerine, in 2 as clear, and in 1 as milky white. Ollier ⁷ (1874) pointed out that the fluid on standing tended to separate into three layers, a bottom layer consisting of broken clumps and flakes with red and white blood cells, a middle clear serous layer and a top layer of floating particles of fat. Riedinger ⁸ (1887) observed mucin and albumin—a slimy, jelly-like fluid containing “animal gum”—and, microscopically, occasional white blood cells. Schlange ⁹ (1887) reported albumin, paralbumin, metalbumin, phosphates, carbonates and large amounts of sugar (with absence of sugar in the urine), fat and, microscopically, red and white blood cells with occasional fat cells. Schrank ¹⁰ (1893) saw many fat globules and yellow flakes. Microscopically he noted clots of fibrin with red and white blood cells and many small droplets of fat and cells in fatty degeneration (*Fettkörnchenszellen*).

Jacoby ¹¹ (1897) noted the presence of small gelatinous clumps. He recorded a chemical analysis of the characteristic exudate as follows: alkaline reaction; water, 91.61 per cent, and solids, 8.39 per cent (nucleo-albumin, 0.87 per cent; serum albumin, 5.61 per cent; fat and extrac-tives, 0.98 per cent, and mineral salts, 0.93 per cent). He drew attention to the resemblance of the fluid to that found in hydrarthrosis. Rondot ¹² (1903) also compared the fluid to that of hydrarthrosis. He described it as follows: specific gravity, 1.026 (at 15 C.); albumin, 55 Gm. per thousand cubic centimeters; no fibrin but a few leukocytes and altered red blood cells. In a second case Rondot noted crystals of cholesterol, leukocytes and a few threads of fibrin; in another case he likened the exudate to the effusion of pleurisy. Scheidler ¹³ (1910) in 2 cases noted red and white blood cells, large cells with fatty degeneration and many droplets of fat. Hartwell ⁴ (1910) in 1 case noted

7. Ollier, cited by Poncet.¹

8. Riedinger, F.: Ueber Ganglion periosteale, in Festschrift, Albert von Kölliker zur Feier seines siebenzigsten Geburtstages, gewidmet von seinen Schülern, Leipzig, 1887.

9. Schlange: Ueber einige seltenere Knochenaffectionen, Arch. f. klin. Chir. **36**:97, 1887.

10. Schrank, W.: Periostitis albuminosa, Arch. f. klin. Chir. **46**:724, 1893.

11. Jacoby, E.: Ein Fall von Periostitis albuminosa, Inaug. Dissert., Bonn, Carl Georgi, 1897.

12. Rondot, A.: La périostite albumineuse, Thesis, Lyon, no. 125, 1903.

13. Scheidler, F.: Zur Periostitis albuminosa (Ollier), Beitr. z. klin. Chir. **68**: 480, 1910.

a clear yellow, thick, gelatinous exudate, rich in plasma cells; in a case with similar exudate, he observed that the fluid contained "pus detritus." He stated that the exudate is often free from cellular elements, contains a high percentage of protein, frequently up to 3 per cent, and often coagulates spontaneously. The tendency to coagulate apparently depends on the presence of leukocytes containing prothrombin. Burckhardt¹⁴ (1911), examining 2 liters of fluid in 1 case, observed that it separated into a light, serous part and a "vitreous" part containing tags and membrane. Mazzini¹⁵ (1932) and many observers before him likened the fluid to synovia. Stropeni¹⁶ (1933) described the fluid as amber colored, stringy and like the white of an egg. Moulouguet and Rousset¹⁷ (1934) noted in 1 case a sticky, "gluey" liquid (1 liter) with a reddish tint and many clots of fibrin. In a second case they saw only a few cubic centimeters of bloody liquid within a large, thick sac. Battle¹⁸ (1904) reported a fluid resembling milk.

Bacteriologic Observations.—Schlange⁹ (1887), the first to report the results of bacterial examination of these exudates, obtained a growth of *Staphylococcus aureus* in 1 case and a negative culture in another. Negative cultures have been reported in 6 cases. Positive cultures have been reported as follows: *Staph. aureus* in 11 cases, *Staphylococcus albus* in 2 and *Staphylococcus* without further specification in 2. Lexer¹⁹ (1898) found streptococci in the case of a child 9 weeks old. Burckhardt¹⁴ (1911) observed in sections a small chain of three or four cocci but obtained no culture. Schrank¹⁰ (1893) in 1 case²⁰ found many

14. Burckhardt, J. L.: Zur Histologie der Periostitis und Ostitis albuminosa, Frankfurt. Ztschr. f. Path. 8:91, 1911.

15. Mazzini, O. F.: Periostitis albuminosa, Bol. y trab. de la Soc. de cir. de Buenos Aires 16:164 (April) 1932.

16. Stropeni, L.: Periostitis albuminosa, Boll. e mem. Soc. piemontese di chir. 3:315 (March) 1933.

17. Moulouguet, P., and Rousset, J.: Les abcès ossifluents chroniques à staphylocoque (périostite albumineuse d'Ollier et Poncet), J. de chir. 44:161 (Aug.) 1934.

18. Battle, W. H.: The Diagnosis of Osteosarcoma of the Long Bones, Lancet 2:582, 1904.

19. Lexer, E.: Zur Kenntnis der streptokokken- und pneumokokken-Osteomyelitis, Arch. f. klin. Chir. 57:884, 1898.

20. His case 2, that of a boy 14 years of age with a previous history of typhoid fever and osteitis some years before. For six weeks swelling of the inner malleolus of the right tibia with abundant, bloody, serous, nontenacious fluid, containing small whitish yellow flakes and many fat globules. At operation a small area of the periosteum was seen to be destroyed, but the underlying bone was not necrotic. Destruction of the periosteum had left a small cavity, the walls of which were covered with soft golden yellow granulations. Low in the cavity a small fistula led to a small bony focus with an abscess containing creamy pus and a small sequestrum. This cavity also was lined with the yellow granulations (color plate, 24).

streptococci and an occasional staphylococcus, the latter predominating in the osteomyelitic pus. L. Dor²¹ (1895) reported observing in a collection of parosteal serous fluid a polymorphous organism with colonies of lemon yellow, the consistency of wax, which slowly liquefied gelatin. He named it *Bacillus cereus citreus*. By intravenous injection of a pure culture of this organism into rabbits, he caused in 1 animal nonsuppurative infectious osteitis, which produced a large exostosis. In another animal he brought about typical periostitis aluminosa. Garré²² (1891) inoculated rabbits with staphylococci from a patient with periostitis aluminosa without producing ill effects. Inoculation with pus from ordinary osteomyelitis, on the other hand, caused the usual signs and lesions of the infection. It was necessary to use large amounts of fluid from periostitis aluminosa to obtain a culture of staphylococci.

Mazzini¹⁵ (1932), in a typical case of periostitis aluminosa, noted, on culture of the gelatinous, stringy, transparent fluid, a gram-positive diplococcus, which grew slowly. Inoculation with the culture produced no local lesion in a guinea pig. A second culture, made several weeks later, at the time of operation, showed no growth. A guinea pig inoculated with the exudate showed no lesion of any kind when killed after two months. Stropeni¹⁶ (1933) on inoculation of a rabbit with a culture of *Staph. albus* made from the exudate in a case of periostitis aluminosa observed a chronic septicemia with many abscesses. There was no local reaction; a curdlike pus was noted, but no bony lesions occurred. In some of the recorded cases, especially the earlier ones, reported by Lannelongue, Nicaise,²³ Rondot¹² and others, there is a strong suspicion that the lesions were tuberculous. Breuer²⁴ (1893) and Sleeswijk²⁵ (1894) described cases in which the condition clinically resembled periostitis aluminosa but was generalized and undoubtedly tuberculous. In Sleeswijk's case the tuberculous character of the symptoms was proved by inoculating the exudate into a rabbit. (Cases of Breuer, Sleeswijk and others in which the tuberculous nature of the disease was unquestioned are not included in the series here reviewed.)

21. Dor, L.: Contribution à l'étude de la périostite albumineuse, des hyperostoses et des exostoses infectieuses, *Arch. prov. de chir.* 4:13, 1895.

22. Garré, C.: Einige seltenere Erscheinungsformen der acuten, infektiösen Osteomyelitis, in *Festschrift zum fünfundzwanzigjährigen Doktor- und Dozenten-Jubiläum von Theodor Kocher*, Wiesbaden, 1891.

23. Nicaise, cited by Bar, E.: De la pathogénie de la périostite albumineuse ou séreuse et d'un nouvel agent pathogène de cette affection, Thesis, Lyon, no. 1017, 1894.

24. Breuer, F.: Ueber sogenannte seröse Abscesse, *Inaug. Dissert.*, Berlin, Emil Ebering, 1893.

25. Sleeswijk, R.: Ueber die sogenannte Periostitis aluminosa (Ollier), *Inaug. Dissert.* (Jena), Amsterdam, J. A. Sleeswijk, 1894.

Pathologic Process.—The earlier observers described the chief changes brought about by periostitis aluminosa as taking place in the periosteum. The collections of exudate have been reported as arising subperiosteally, intraperiosteally and extraperiosteally. They have been seen free in the soft tissues, with no definite encapsulation, and have been seen enclosed in a more or less definitely formed sac. At times the exudate is described as infiltrating the periosteum, muscles and fascia, changing these structures into a succulent, soggy mass (*épanchement*, *Flüssigedurchtränkung*). Cases have been reported in which the exudate was associated with no demonstrable lesion of the neighboring bone. Other cases in which the periosteal changes and the exudate were secondary to osteitis and osteomyelitis are included in the literature. The existence of two separate lesions in close proximity has occasionally been described.²⁰ Schlange⁹ was the first to draw attention to the association of the disease with osseous lesions, and because of these lesions he proposed the name "osteomyelitis non purulenta." The color plate represents an attempt to classify and illustrate diagrammatically the various pathologicoanatomic conditions as they are described in the available literature. In 57 cases the observations were made by incision, which was frequently preceded by aspiration. In 5 cases only was aspiration alone done—Takvorian (1878), Perrier (1883), Rondot¹² (1903, case 1), Scheidler¹³ (1910, case 2) and Stuparich²⁶ (1902). In 3 reports there was no note as to aspiration or incision.

Cases of serous inflammation of a bone following an attack of suppurative osteomyelitis in the same bone have been reported by Poncet¹ (case 3), Garré²² and Deutschländer.²⁷ Donati²⁸ reported a case of periostitis aluminosa of a femur, which showed recovery after operation and was followed a few years later by acute osteomyelitis of the same bone. Periostitis aluminosa in one bone with suppurative osteomyelitis simultaneously in another bone of the same patient has been noted by Lipschitz²⁹ (1902) and Muhl³⁰ (1893). Rosenbach reported a case of periostitis aluminosa occurring simultaneously in a rib and a femur. Cases of periostitis or osteoperiostitis aluminosa in persons with a history of osteomyelitis have been reported by Hartwell,⁴ Stropeni¹⁶ and Moulouguet and Rousset.¹⁷ A history of typhoid infection was

26. Stuparich: Ein Fall von Periostitis aluminosa, Wien. med. Presse **43**: 411, 1902.

27. Deutschländer: Ostitis aluminosa, München. med. Wchnschr. **8**:379, 1905.

28. Donati, cited by Stropeni.¹⁶

29. Lipschitz, R.: Zur Kenntnis der Periostitis aluminosa, Inaug. Dissert. (Freiburg), Berlin, M. Liebmann, 1902.

30. Muhl, A.: Ueber Ostitis und Periostitis nonpurulenta (Periostitis aluminosa, Ollier), Inaug. Dissert., Bonn, E. Heydorn, 1893.

given in the cases of Riedinger⁸ (1887), Schrank¹⁰ (1893), Rondot¹² (1903) and Hartwell.⁴ Schrank (1893) stated that when these lesions are associated there is never an organic connection between them.

Formation of the Cyst and the Exudate.—The formation of cavities in the soft parts resulting from the characteristic accumulations of fluid in the older reported cases is only vaguely described. Lannelongue (1878) and Nicaise²³ (1879), who had an opportunity to examine stumps left after amputation of tuberculous joints, reported the fluid as being contained in small cavities within the thickened periosteum. Riedinger⁸ (1887) denied that the cysts described were true cysts in the anatomic sense and therefore suggested the name “ganglion periostale” or “parostale” for these saclike structures. Schlange⁹ (1887) described the accumulation of fluid as occurring in the following possible ways:

1. The fluid gathers under the periosteum and lifts it from the bone. In this case the bone lies uncovered in the bottom of the cyst.

2. The fluid gathers in the layers of the periosteum, breaks through their thin sheaths and develops in a cystic sac within the periosteum. In this case the bone is not exposed, but the periosteum will appear thin in the bottom of the cavity.

3. The fluid is derived *ab initio* from the outer aspect of the periosteum, or a subperiosteal or endoperiosteal accumulation of fluid breaks through early. After this, presumably because of diminished local reaction in the tissue, a diffuse, edematous swelling may form instead of a cyst. Especially likely to occur are the transudations (*Flüssigedurchtränkungen*) of the outer periosteal layers or even of the nearby structures of muscle and connective tissue described in some cases.

After the sac has once formed, its inner lining provides for its own persistence through its secretory activity, as this activity is at least as great as its resorptive powers. When there is an encapsulated exudate, the sac adheres to the bone on one side only and to a varying extent. Its walls have no definite boundaries and without macroscopic textural changes pass into the thickened periosteum. The thickness of the wall of the sac may reach several centimeters. On its exterior surface it is not sharply separated, but its fibrous tissues lose themselves in the surrounding perimysial and intermuscular connective tissues. Its inner wall is smooth and lined with a thin, veil-like layer of brownish red granulation tissue. The cavity need not be globular or ovoid but may assume complicated forms.

Lipschitz²⁰ (1902) also assumed the occurrence of a direct serous exudate from the abscessed membrane. In the beginning a small amount of pus is formed. This process is rapidly depressed, either because the cocci are weak in virulence or numbers and therefore impeded in their further development or because the formation of pus encounters resist-

ing tissues. From this point on, there is no further wandering out of leukocytes but rather a transudation of serum. Scheidler¹³ (1910) in speaking of cysts with smooth bone exposed, without periosteal covering beneath them, stated that these cysts result from periosteal proliferation and inflammatory reaction in the surrounding tissues. If periosteal proliferation does not keep pace with the increase of fluid, the fluid breaks through into the surrounding tissue, which reacts to the irritation thus produced. Eventually the periosteum reattaches itself to the bone, and the original osseous focus heals. A similar picture is seen when the fluid escapes from a layer of the periosteum. The lesion then heals, leaving a cavity at its bottom lined with proliferated periosteum and connective tissue.

Mazzini and Brachetto-Brian³¹ (1933) expressed the opinion that permanent hyperemia and an added perivascular inflammatory exudative process in the layers of the periosteum cause a transudate of plasma. This collects in the layers of the traumatized periosteum. In many reported cases since Schlange's first more detailed exposition, the sac has been described as thick—up to 3 cm. or more. The anatomic observations suggest possible formative processes as outlined by him and others, including Burckhardt¹⁴ (1911) and Stropeni¹⁶ (1933). Stropeni described the sac as thick, with an inner capsule lined with granulations. Moulonguet and Rousset¹⁷ (1934) noted a thick sac the size of a kidney, the outer surface of which was smooth and regular. When it was opened it disclosed a limited cavity with a red, fungoid lining, which contained fibrinous clots and a few cubic centimeters of bloody liquid but no pus. *Staph. aureus* was obtained on culture.

Histologic Picture.—In the first reported histologic examination in a case of periostitis aluminosa (1878), Lannelongue observed that the periosteum covering the bone was thin but showed no change in its texture. Schlange⁹ (1887) saw giant cells in the sac, and "further examination of the wall of the cyst showed a firm, cell-poor fibrous tissue, while the brown inner layer consisted of granulation tissue." Schrank¹⁰ (1893) noted thickening of the periosteum, which involved, to some extent, both layers and which was due to hyperplasia. Near vessels were observed larger foci of round cells; the fibrillar connective tissue was distended with fluid. Battle¹⁸ (1904) reported granulation tissue viewed microscopically and stated that there was no pus. Pickrell and Schmidt³ (1910) expressed great doubt as to the micropathologic condition, remarking that the microscopic picture is hardly distinguishable from that of sarcoma. Sections in 2 cases "indicate fibro-chondro-osteoma." Hartwell⁴ (1910) noted chronic inflammatory changes.

31. Mazzini, O. F., and Brachetto-Brian, D.: Periostitis aluminosa. Bol. y trab. de la Soc. de cir. de Buenos Aires 17:13 (April) 1933.

Burckhardt ¹⁴ (1911) was the first to give a detailed histologic study and review of the condition up to his own time. In the case reported by him, the microscopic examination showed subacute to chronic inflammation.

We find a poorly vascularized granulation tissue, which, so to speak, consisted only of normal and degenerated (fatty) plasma cells. Among these one sees some small foci of leukocytes but nowhere formation of abscess. Very striking, however, was the fatty degeneration and the formation of tissue, in places, from cells which conformed to those described as granular fat spheres (*Fettkörnchenkügelchen*) but were devoid of fibrillar supporting substance. Aside from the fatty degeneration, we find rarely another transformation of plasma cells, namely, the formation of Russell bodies. . . . We wish to emphasize that we found these bodies only in plasma cells and that in this case there could be no thought of their origin from red blood cells. These observations conform to those described as made on pathologic granulation tissue—"sequestal granulations." The microscopic characteristics, as contrasted with those of normal granulations in wounds, are especially the large fluid content, the lack of polynuclear leukocytes and fibrin and finally the fatty degeneration of the cells.

Burckhardt reported seeing some giant cells also.

In the case described by Mazzini and Brachetto-Brian ³¹ (1933) the cavity was lined with pale fibrous tissue, which continued to the periosteum and its normal limits. In the bottom of the cavity the tibia, in a denuded area, was covered with a delicate layer of granulation tissue. The external layer of a portion of the periosteum removed for examination was formed of loose connective tissue, with cells, dilated vessels and moderate exudative inflammation about the vessels (polymorphonuclears and lymphocytes). The internal layer consisted of a myxomatous structure containing many small vessels and dilated capillaries. Adhering to its superficial surface was albuminous, homogeneous and amorphous matter with the appearance of colloid. In the myxomatous tissue were small areas of "osteogenesis directa." There were noted two processes, a hyaline degeneration of the connective tissue and an exudative inflammation about the vessels, occupying the distinct layers. In the vessels were seen deposits of yellow pigment. Stropeni ¹⁶ (1933) described the thickened sac as containing granulation tissue and infiltrated with plasma cells. Moulouguet and Rousset ¹⁷ (1934) stated that the wall of the sac is a pyogenic membrane infiltrated with polymorphonuclear leukocytes, i. e., an infective granuloma.

Ganglion.—Many of these cystlike formations, especially those near joints, strikingly resemble true cystlike extensions from neighboring synovial structures. Therefore, some have questioned their origin from lesions of periostitis albuminosa. Thus, Jacoby ¹¹ (1897) expressed a suspicion that Riedinger ⁸ and Schreiber ³² were dealing with diver-

32. Schreiber: Ganglion periostate, München. med. Wchnschr. 40:778 (Oct.) 1887.

ticula from a joint capsule. Plenz³³ (1929) under the title "Hygroma Migrans?" detailed a case of a cyst along the anterior aspect of the tibia which produced superficial bony spicules on that bone. He was able to follow the growth up to (but not into) a joint and decided it was a hygroma. He also expressed a strong suspicion that some cases reported in the literature as periostitis aluminosa were, in reality, instances of hygroma. His investigations showed that the contents of the sac may speak for hygroma, as well as for periostitis aluminosa. Gelatin always speaks for hygroma, even if from its location it does not appear to be associated with a bursa.

Trauma.—The incidence of trauma and the part it plays in the causation and production of periostitis or osteoperiostitis aluminosa have been variously reported and interpreted in this series of cases. Of the cases in which trauma was mentioned in the histories, it was noted as absent in 32 and present in 16. Pickrell and Schmidt³ (1910) expressed the opinion that in the 3 cases reported by them the condition was traumatic in origin and noninfectious. They stated that the inflammation may be produced by a single severe blow over a bone or by a crushing injury to the periosteum. In the young it may be produced by a compressive force applied to the ends of a bone, springing the bone, with resulting detachment of a small area of periosteum. Likewise repeated slight injuries to an exposed bone may produce chronic periostitis. Reh³⁴ (1922) referred to a case reported by Heineman of non-infective post-traumatic periostitis and added that similar changes may occur after injury in old hematomas. He expressed a doubt that such a process could be classed as periostitis aluminosa Ollier. Injury, however, according to Reh, is an important factor in periostitis aluminosa. Without local damage, primary periostitis, he stated, is unthinkable except on the assumption of an anomaly of blood supply or other disturbance of nutrition through toxic or chemical influences. Mazzini and Brachetto-Brian³¹ (1933) based a diagnosis of periostitis aluminosa traumatica on a history of trauma, a sterile culture and the results of microscopic examination of the sac. They pointed out that trauma produces a permanent hyperemia of the whole vascular system of the periosteum. To this is added a perivascular inflammatory exudative process, and abundant new capillary vessels are formed in the inner layers of the periosteum. The permanent local congestion causes a transudate of plasma, which by and by collects in the layers of the traumatized periosteum.

33. Plenz, P. G.: Periostitis aluminosa oder Hygroma "migrans"? Zentralbl. f. Chir. **31**:1947 (Aug.) 1929.

34. Reh, H.: Periostitis infectiosa (P. rheumatica), Deutsche Ztschr. f. Chir. **169**:168, 1922.

The Infection.—Some of the earlier writers, among them Perrier (1883), Duplay³⁵ (1880) and Roser³⁶ (1887), assumed a rheumatic diathesis as the underlying cause of periostitis aluminosa. This assumption was probably based on the resemblance of the fluid to the exudate of a joint and the previous or associated occurrence of acute or subacute rheumatic polyarthrititis. Most writers, especially those whose reports have appeared since that of Schlange, have admitted the infectious character of periostitis aluminosa, which Pickrell and Schmidt³ and Mazzini,¹⁵ among the more recent writers, have denied. Most writers have attributed the infection to the ordinary pus organisms, namely the staphylococcus and the streptococcus, and much speculative attention is given to the seat of the primary focus of the infection.

Seat of the Lesion.—Periostitis aluminosa was first described, by Ollier and Poncet,¹ as a purely periosteal lesion. Lannelongue, who examined the condition in an amputated limb, observed no bony lesion. Ollier expressed the thought that in most of the earlier cases the disease was chronic from the beginning but stated the assumption that it may begin acutely with pain and fever. In cases of the latter description the acute symptoms subside in a short time, to be followed by a chronic course. Cartuffe³⁷ (1883) proposed the name "periostitis exudativa," ". . . showing that this disease is not osteomyelitis, although we do not know but that the former disease might under certain circumstances lead up to the latter." Hartwell⁴ (1910) said his cases demonstrated that periostitis aluminosa is not a specific disease but the expression of irritation of the periosteum by an infecting organism of low grade virulence. Such an organism produces the characteristic albuminous exudate rather than pus. He added that it is not known why this is so.

Schlange⁹ (1887) expressed the opinion that in these cases the germ of osteomyelitis may be present in smaller amounts or in an attenuated phase or attack a person less predisposed. In short, conditions are unfavorable for the production of a more intense inflammation and the disease, therefore, is subacute from the beginning. On the other hand, the inflammation may be more active in the beginning but, because of early encapsulation, be hindered in its full activity. This view suggests only a difference of degree between the purulent and the non-purulent form of osteomyelitis. Jaksch³⁸ (1890), Schrank¹⁰ (1893),

35. Duplay, M.: Périoste externe rhumatismale (périostite albumineuse d'Ollier), Arch. gén. de méd. 146:728, 1880.

36. Roser, W.: Zur Lehre von der Periostitis aluminosa, Zentralbl. f. Chir. 14:929 (Dec.) 1887.

37. Cartuffe, cited by Dupuis.²

38. Jaksch, R.: Zur Lehre von der Periostitis aluminosa, Wien. med. Wchnschr. 49:2097 (Dec.) 1890.

Ehrich³⁹ (1896), Lexer¹⁹ (1898), Lipschitz²⁹ (1902), Deutschländer²⁷ (1905), Reh³⁴ (1922), Stropeni¹⁶ (1933) and Moulonguet and Rousset¹⁷ (1934) all expressed more or less agreement with Schlange. They stated the assumption that the primary lesion originates in the periosteum, below the periosteum, in the cortex or in the medullar cavity. The primary seat of the infection is obviously difficult to determine, as exposure of bone or a cortical lesion does not prove that the bone was primarily affected. Likewise, an apparently intact periosteal covering does not necessarily speak for a nonosseous origin of the lesion. A study of the color plate suggests the presence of various possible primary foci in the available recorded cases. Moulonguet and Rousset¹⁷ (1934) described their cases as an attenuated form of osteomyelitis and suggested the term "forme fruste." They quoted Lecine and Leriche as declaring the condition to be cortical osteitis, very superficial and highly localized.

Tuberculosis.—Roser³⁶ (1887) expressed a suspicion that in some of the earlier cases described as instances of periostitis albuminosa the condition was really tuberculous, as in those of Nicaise²³ and Lannelongue. He stated the belief, however, that cases of tuberculous periostitis occur in which the exudate is watery or watery-purulent. Legiehn⁴⁰ (1890) expressed the opinion that in 2 of the 15 cases reported up to his time the condition was tuberculous. The cases of Breuer²⁴ (1893) and Sleeswijk²⁵ (1894) were obvious cases of generalized tuberculosis. Rondot¹² (1903) reported the condition in his third case as periostitis albuminosa in a hip which had previously been the seat of tuberculosis. Riedel made the following annotation at the end of Sleeswijk's thesis:²⁵

It is well known that osteal or periosteal tuberculosis may cause a serous exudate—it is very probable that many earlier cases described as periostitis albuminosa may have been tuberculosis. In general it will be held that "osteitis and periostitis albuminosa" are the result of an attenuated staphylococcic, streptococcic or other infection. If one were to include tuberculosis as an etiologic factor, one would call the condition "osteitis or periostitis albuminosa tuberculosa."

Most writers, especially the more recent ones, have stressed the importance of considering tuberculosis in the diagnosis of these conditions. Moulonguet and Rousset¹⁷ (1934) warned that "cold abscesses are not all tuberculous." In 1 of their cases, the nontuberculous character of the disease was established after the patient had been for years under treatment (mistakenly) for a tuberculous disease of the hip. Roser³⁶

39. Ehrich, E.: Ueber latente Eiterherde im Knochen, München. med. Wchnschr. 43:693 (July) 1896.

40. Legiehn, F.: Ueber die sogenannte Periostitis und Ostitis albuminosa (Ollier), nebst Mittheilung zweier Krankengeschichten, Inaug. Dissert., Königsberg, M. Liedtke, 1890.

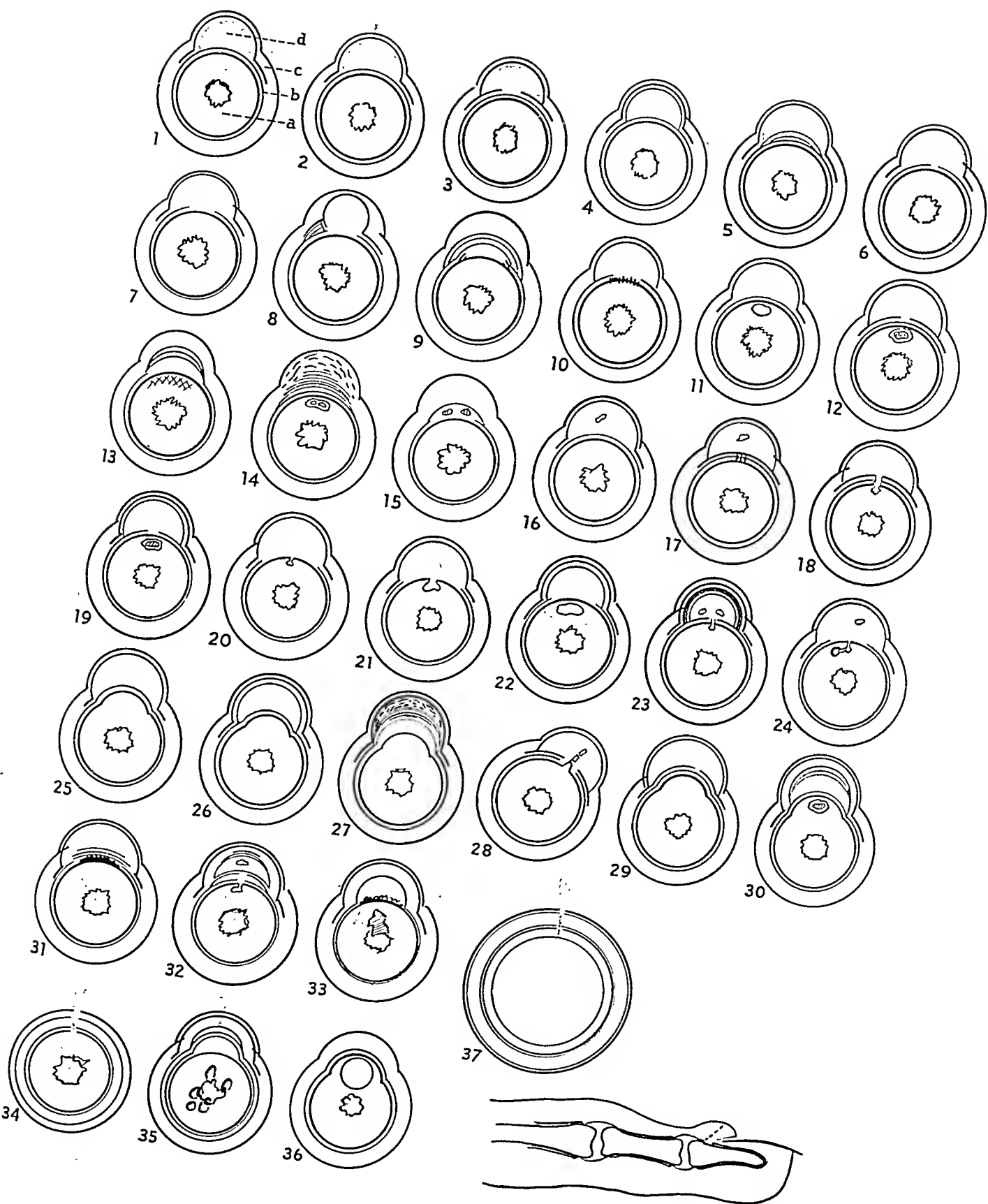
EXPLANATION OF COLOR PLATE

a represents a cross section of a long bone (black); a bulge in this outline (as in 25) represents cortical thickening of the bone; roughening of the cortical surface and formation of cavities with and without sequestrums are indicated by special markings; in 37 the diagrammatic representation is relatively larger to convey the idea of an enlarged bone with cortical thinning and a central cyst. *b* represents periosteum (red). *c* represents the soft parts surrounding bone. *d* represents the cystic accumulation (green) in the soft parts or within the bone.

The numbers under diagrammatic figures 1 to 37 represent the various types of lesions as described in the literature as follows:

1. Bar, Rondot (case 6), Scheidler (case 1), Hartwell (case 3). 2. Duplay. 3. Moulouguet and Rousset (case 1). 4. Lannelongue (cases 1 and 2), Rosenbach, Perrier. 5. Rondot (case 4), Roser. 6. Mazzini, Cazin. 7. Jacoby, Legiehn (case 1). 8. Hartwell (case 2). 9. Riedinger, Nicaise, Stropeni, Schreiber, Poncet (case 3). 10. Poncet (case 2). 11. Lipschitz. 12. Moulouguet and Rousset (case 2). 13. Hartwell (case 3), Lecine and Leriche. 14. Schlange (case 2), Scheidler (case 2). 15. Jaksch. 16. Kuth (case 2). 17. Mennen. 18. Muhl. 19. Czerny. 20. Schrank (case 1). 21. Ollier. 22. Savariaud. 23. Schlange (case 1). 24. Schrank (case 2). 25. Albert. 26. Terrier. 27. Dupuis. 28. Hartwell (case 1), Pickrell and Schmidt (cases 1 and 2). 29. Reviglio. 30. Riedel. 31. Burckhardt, Battle. 32. Schlange (case 3). 33. Legiehn (case 2), Beekenkamp. 34. Lexer. 35. Deutschländer, Garré. 36. Schlange (cyst). 37. Ehrich (cyst).

The diagrammatic sketch in the lower right corner represents the finger in case 4, showing the site of the lesion and the sinus (green).



(1887) took issue with Riedinger and Schlange, maintaining that the condition (periostitis aluminosa) as described is not a clinical entity. Schrank¹⁰ (1893) expressed the thought that in the reported cases it did not present a uniform, sharply defined clinical picture. If the cases were to be regarded as instances of a single disease, he stated, the limits of the definition would have to be widened considerably. Sleeswijk²⁵ (1894) pointed also to the difference in opinion regarding the seat of the disease, the nature of the exudate and its causation.

Origin and Character of the Exudate.—Since Poncet's first publication, much interest has been shown and much speculation indulged in relative to the origin of the peculiar exudate. Ollier stated the assumption that the fluid arises from either the bone or the periosteum. Duplay³⁵ (1880) expressed the opinion that the serous exudate is the first stage of every inflammation; in this case the inflammation remains in that stage, not going on to suppuration. This exudate may originate outside and independent of the periosteum, and is due to a rheumatic diathesis. Riedinger⁸ (1887) stated the thought that under certain conditions the periosteum can put forth a product as tendon sheaths put forth ganglions. He saw the same chemical characteristics in the fluid of the ganglions produced by the tendon sheaths as in the accumulated fluids of periostitis aluminosa. He expressed the opinion that periostitis does not represent an inflammation in the ordinary sense of the term. It consists rather of a perspiring (*Ausschwitzung*) of fluid from the involved soft tissues.

Schlange⁹ (1887) stated his assumption that the fluid originates from an osseous lesion. He expressed the opinion that periostitis aluminosa is not the result of chronic and persistent osteomyelitis in the sense that the peculiar fluid is a modification of an osteomyelitic abscess. That is, it is not the product of a gradual change of pus into serum. Against this is the observation of serous fluid early in the course of the disorder and the lack of foundation in pathology for such a supposition. He stated the belief that the characteristic exudate is due to the organisms of suppurative osteomyelitis, which are present in small numbers in a phase of diminished virulence. For these reasons, he said, or because of the lessened susceptibility of the person attacked, they do not form ordinary pus.

Vallert⁴¹ (1890) stated that the exudates are due to abscesses which have originally a purulent content but gradually undergo a mucoid metamorphosis. Breuer²⁴ (1893) expressed his feeling that the occurrence

41. Vallert, J.: Ueber die sogenannte Periostitis aluminosa nach Erfahrungen aus der chirurgischen Klinik zu Halle, Samml. klin. Vortr., no. 351, 1890 (Chir. no. 108, pp. 3355-3372); cited by Kaufmann, E.: Lehrbuch der speziellen pathologischen Anatomie, ed. 6, Berlin, Georg Reimer, 1911, vol. 2, p. 689.

of fat, calcium and phosphates speaks for an osseous origin of the fluid. The exudate can, however, develop independently from the walls of the cyst. Lipschitz ²⁰ (1902) said that the fluid is derived as a direct serous exudate from the membrane of the abscess. In the beginning a small amount of pus is formed, a process which is rapidly depressed, with no further wandering out of leukocytes but with more transudation of serum. Whether the mucoid character of the exudate is due to degeneration of elements in the wall of the abscess or, as Vallert would have it, to a mucoid metamorphosis of the original pus is undecided. Garré,²² in support of Vallert's theory, offered his observation of a case in which the first aspiration showed pus and eight weeks later, on incision, mucoid exudate was found. He stated the belief that pus can be so thinned by a transudate of serum or lymph as to give rise to a rapid increase in the swellings. In a case reported by Jacoby ²¹ (1897) in which a culture of *Staph. aureus* was obtained the typical serous exudate became purulent a few days after incision for drainage. Muhl ³⁰ (1893), Ehrich ³⁹ (1896), Lexer ¹⁹ (1898) and Hartwell ⁴ (1910) offered no explanation of the formation of the exudate. Schrank ¹⁰ (1893) supported Schlange and expressed the thought that the exudate arises from a degenerative process of the granulations rather than from a fatty or mucoid degeneration of the pus.

Burckhardt ¹⁴ (1911), confirming the microscopic observations of Schlange and others, stated that the phenomena which they observed conform to those described by Reinbach ⁴² as pathologic granulation tissue (*Sequestergranulationen*). Reinbach pointed out a form of inflammation on the surface of the body in which the amount of serous exudate is many times that of granulation in healthy wounds. In the exudate of such inflammations, he said, the newly formed cells "swim." The cause of this process lies in the fact that the inflammatory stimulus is not strong enough to call forth a sufficient proliferation of tissue. The leukocytes, therefore, cannot be lured on (*angelockt werden*) by the stimulating agent of the inflammation. The formation of the exudate may be explained by an abnormal permeability of the walls of the vessel or, per contra, by an activity of their cells. The first explanation can, according to Burckhardt, be drawn to the support of his case in view of the fatty degeneration of the endothelial structures. Kocher and Tavel ⁴³ said that the serous exudate results from fatty degeneration of granulation tissue. Aschoff ⁴⁴ stated his feeling that periostitis albuminosa follows periostitis purulenta, in which granulation tissue secretes

42. Reinbach: Untersuchungen über den Bau verschiedener Arten von menschlichen Wundgranulationen, Beitr. z. path. Anat. u. z. allg. Path. **30**:102, 1901.

43. Kocher and Tavel, cited by Kaufmann, E.: Lehrbuch der speziellen pathologischen Anatomie, ed. 6, Berlin, Georg Reimer, 1911, vol. 2, p. 689.

44. Aschoff, cited by Reh.³⁴

serous fluid. Reh ³⁴ (1922) expressed his inclination to Vallert's view; he stated the belief that no primary periostitis aluminosa, as such, exists. Stropeni ¹⁶ (1933) expressed his acceptance of Vallert's view as to the origin of the fluid. Mazzini and Brachetto-Brian ³¹ (1933), as noted in the section entitled "Trauma," attributed the formation of fluid to permanent hyperemia of the vascular system of the periosteum and to perivascular inflammation.

Breuer ²⁴ (1893) and Sleeswijk ²⁵ (1894) drew attention to the change of the fluid in tuberculous abscesses from a purulent to a mucoid form after repeated injections of iodoform and glycerin. Thereby they suggested the possibility of similar changes in the exudates here in question. Scheidler ¹³ (1910) quoted Henle, who stated the belief that pus will be transformed to a serous exudate only as a result of treatment, such as repeated aspirations or injections. Scheidler further stated that there exist no reported observations of a case in which serous abscesses were associated with tuberculosis. The origin of the fat seen in many of the exudates was attributed by Ollier ⁷ (1874), Schlange ⁹ (1887), Roser ³⁶ (1887), Muhl ³⁰ (1893) and others to the bone (marrow). Schrank ¹⁰ (1893), Burckhardt ¹⁴ (1911), Kocher and Tavel,⁴³ on the other hand, attributed it to fatty degeneration of the granulation tissue. The question, therefore, has been: Is the exudate serous from the beginning, or is it changed pus? Can the usual pus organisms under certain conditions produce a serous exudate or not?

Roentgenographic Examination.—Rondot ¹² (1903) was the first to record the use of roentgen rays in the diagnosis of this condition. The roentgenogram, however, was too poor to be of use. Battle ¹⁸ (1904), with the aid of roentgen rays, was able to determine an infectious periosteal thickening and differentiate it from malignant osseous tumor. Deutschländer ²⁷ (1905) in a case of osteomyelitis aluminosa following open fracture of a bone observed typical osteomyelitic foci roentgenologically in the medullar cavity. Scheidler ¹³ (1910) pointed out that the roentgen examination may reveal the type of lesion and indicate what extent of surgical intervention is desirable. He indicated that because of excessive fluid or great thickening of the wall of the cyst the roentgenogram may appear poor. The plates show the extent of the fluid in the soft parts, but for better bony detail it should be aspirated and the roentgen examination repeated. In 1 of his reported cases the roentgenogram showed thickening of the cortex over the inner and outer aspects of the bone and extensive shadow of the soft part. A depression in the upper third of the femur was seen only after evacuation of the fluid, but there was no lesion in the medullar cavity. In a second case, there was noted a localized bony focus near the upper epiphysis of the humerus, leading to an area of destruction in the head of the bone as

well as to a lesion near the epiphysis of the acromion. Here again he pointed out the distinct difference in the roentgenograms taken before and after aspiration. Pickrell and Schmidt³ (1910) in 3 reported cases noted on roentgen examination a marked bony proliferation, in 1 case "resembling myositis ossificans" and in another presenting a fusiform shadow.

In Hartwell's case¹ (1910) the roentgenograms suggested tumor. Burckhardt¹⁴ (1911) observed in the distal end of a femur, reaching to the middle of the bone, a superficial proliferation 2 to 3 mm. in thickness, casting a definite shadow. The compact part of the distal end of the bone was noticeably smaller and showed toward the medullar cavity an irregular contour. The medullar cavity presented a turbid shadow, which in places was not sharply separated from the compact bone. Mazzini¹⁵ (1932) reported negative results from roentgen examinations. Stropeni¹⁶ (1933) in a case of involvement of the skull reported the roentgenogram as showing perfect integrity of the frontal bone. He quoted Revigilio, who in roentgenologic studies found areas of rarefaction in trabeculae, due to demineralization, which produced in the roentgenogram an almost homogeneous appearance of the bone. The trabeculae were smaller than those of normal bone, and periosteal hyperactivity with irregular calcification was noted. Revigilio stated also that if macroscopic examination of the bone shows periosteal involvement, the lesion, even though not evident, is nevertheless primary in the bone as attenuated osteomyelitis without destruction. Moulouguet and Rousset¹⁷ (1934) in roentgenograms taken in 1 case saw an osteophyte on the ilium between the anterior inferior spine and the acetabulum. There was no bony atrophy, and the hip joint was apparently normal; in a second case they noted lamillary osteitis of the ilium above the acetabulum. They stated that in general roentgen examination in cases of periostitis aluminosa will show absence of decalcification and production of new bone.

REPORT OF CASES

The following cases are the personal observations to which reference was made in the introductory paragraph of this paper:

CASE 1.—Mrs. L. S., aged 36, was seen in November 1931, complaining of pain and soreness in the right calf, which she stated began about one year previously. The soreness was accompanied by a slight swelling of the right calf and caused intermittent lameness. About two months before, a swelling began in the back of the right knee (popliteal space), which was not painful or tender to touch or pressure but was gradually increasing. The familial and the personal history revealed nothing of interest. There was no history of injury, but the patient admitted falling frequently because of "weak ankles." There was no history of infection, except that some years previously she had had what she thought was inflammatory rheumatism in the right knee and left ankle.

Examination showed a well developed, well nourished woman with the appearance of good health and no abnormalities other than the swelling and lameness. The temperature was normal, the pulse rate 84 and the blood pressure 122 systolic and 78 diastolic. The Wassermann reaction was reported negative. The right calf was slightly larger than, but otherwise no different from, the left. In the right popliteal space was noted a swelling about the size of a goose egg, firm but showing some resiliency on pressure, like a tightly filled cyst. The skin and soft tissues over this swelling appeared normal but possibly slightly warmer than the surrounding tissues. Neurologic examination of the lower extremities showed no abnormality. A roentgenogram of the knee, made in two positions, showed only the shadows of the soft parts, with a small, irregular denser shadow in its outer limits in the lateral view (fig. 1).

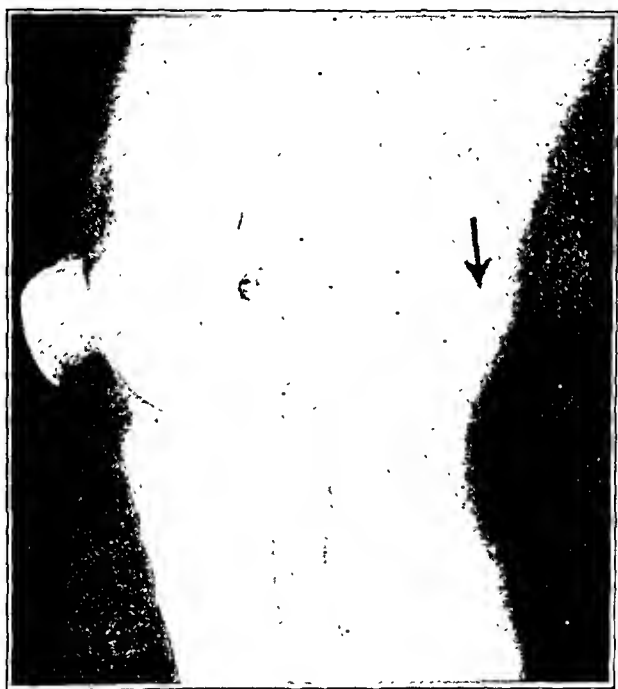


Fig. 1.—Roentgenogram made in case 1 (Mrs. L. S.). The arrow points to the sequestrum.

It was assumed that the patient had a cyst or ganglion arising from synovial structures in or about the knee joint or possibly a malignant tumor. Therefore, on November 19, the affected part was explored surgically by a longitudinal mid-popliteal incision. Under the superficial fat, a slightly oval tumor, measuring about $3\frac{1}{2}$ by 4 inches (9 by 10 cm.), was exposed. It was moderately adherent to the surrounding soft structures and was grayish white over its external surface, with definite fluctuation. After it was freed by sharp and blunt dissection, the external popliteal nerve was seen to pass over the tumor and the large vessels to pass along its inner side. The capsule of the tumor was observed attached by dense scar tissue to the surrounding soft parts at its inner and distal surface and to the femur at its proximal end. While being removed, the tumor (cyst) broke, evacuating a large amount of clear brownish fluid, thick, sticky and resembling

synovia. With the fluid, escaped a small, irregularly shaped piece of necrotic bone (sequestrum). The cyst was completely removed. No evidence of disease was seen in the exposed portion of the femur, where the sac had been intimately connected with the bone by denser scar tissue.

Results of pathologic examination were reported by Dr. George Berdez, of St. Mary's Hospital: "Macroscopically the specimen is a sac-shaped structure, measuring 8 by 6.4 cm. The wall of the sac measures from 0.5 to 1.2 cm. in thickness and is formed of masses of scarlike fibrous tissue. Its internal surface is extremely congested and shows diffuse hemorrhages. At one of its extremities, its external surface shows a piece of striated muscle, which is involved in the mass of scarlike connective tissue. The sac still contains a small amount of hemorrhagic, purulent material and a hard specimen of irregular shape, measuring 1 by 1 by 0.3 cm., apparently formed by bony tissue. Microscopically the wall of the sac is seen to be formed of rather tough connective tissue. Its internal surface is lined with cellular granulation tissue, which is densely infiltrated with lymphocytic, plasmatic and polymorphonuclear cells. In places there are diffuse hemorrhages and deposits of hemosiderin. No tubercles are observed. Sections through the smaller piece of bone show that it is formed of irregular, thin, anastomosing bony trabeculae; the medullar spaces are filled with necrotic fibrous and adipose tissue."

No bacterial examination was made. The wound healed by primary union, and the patient reported herself fully recovered in July 1936.

This case is similar in practically all respects to a number of the recorded cases, resembling, especially in the location of the process, the cases of Reviglio,⁴⁵ Savariaud and Mennen.⁴⁶ The location, in the popliteal space, suggests the possibility of hygromatous extension from the knee joint or the neighboring tendons or bursas. The entire independence of the process from the knee joint and bursal structures was demonstrated. The initial lesion was either a primary periostitis or primary cortical osteitis with separation of a small, flat sequestrum, followed by healing. Scar tissue was formed in the bone cortex and the periosteum and the fluid and sequestrum encapsuled. The symptoms appeared gradually and persisted for ten months before swelling was noticeable in the popliteal space. This suggests that most of the exudate accumulated during the latter two months, after the osseous or periosteal lesion healed and the sac separated from the original focus of infection (color plate, 17). The excess exudate would most likely be derived from the inner lining of the sac as a "secretion," as has been suggested by Schlange⁹ and others. (Schlange's view is discussed in the section entitled "Formation of the Cyst and the Exudate.") It is probable likewise that the thickness of the sac and the tendon within it increased more rapidly during the latter two months. Whether the exudate was serous or purulent from the beginning cannot be determined in this case. Trauma does not appear to have been a factor. The infectiousness of the

45. Reviglio, cited by Stropeni.¹⁶

46. Mennen, W.: Zur kenntnis der Ostitis albuminosa, Inaug. Dissert., Jena, G. Neuenhahn, 1892.

disorder is evident from the histologic examination of the sac and the character of the sequestrum. The history of "inflammatory rheumatism" in the right knee and left ankle suggests a previous infection, which possibly caused the lesion in the distal end (metaphysis) of the femoral shaft. Had this subacute type of lesion in the cortical bone been in mind, the significance of the small shadow noted roentgenographically in the soft parts might have been appreciated. In that case it is possible that the correct diagnosis could have been made preoperatively.

The case of Mennen ⁴⁶ (1892) holds a considerable degree of interest in connection with case 1 here reported:

A woman aged 21 complained of gradual onset of mild pain during one and one-half years, with swelling in the right popliteal space of about the same duration. Two aspirations preceded the incision, one fourteen or fifteen months after the onset and a second three or four months later. At the first aspiration there was a clear light fluid and at the second nearly a liter of yellow, transparent albuminous fluid. The latter was not stringy and contained small white particles which were seen microscopically to consist of fibrin with numerous white blood cells. Two weeks after the second aspiration, at the time of operation, the cyst had again filled to its original size with a clear yellow serum. At operation it was found to be impossible to remove the sac, because of surrounding dense adhesions, and treatment therefore was limited to simple incision and drainage. The walls of the sac measured from 1 to 1.5 cm. in thickness and were dense, with areas of localized thickening. Lying free in the sac, near the lateral condyle, was a sequestrum the size of a pea. No defect was noted in the bone, which was covered completely by periosteum (color plate, 17). The periosteum and also the whole inner wall of the sac were covered with soggy granulations of satin-like texture. In this case, from the behavior of the exudate after each evacuation, it is evident that it was derived from the wall of the sac.

CASE 2.—L. L., a waitress, aged 19 and single, consulted Dr. W. C. Martin for disability of the left elbow and forearm following an accidental injury on Nov. 30, 1935. She stated that she struck the back of her left elbow against a banister and that six days later a small swelling appeared over the front of the left forearm. The swelling was seen just distal to the bend of the elbow. She complained of soreness over the back of the left elbow at the distal end of the upper part of the arm and over the inner condyle of the humerus. There was also moderate soreness in a small swollen area on the flexor surface of the left forearm an inch or so distal to the elbow. I saw the patient on December 27, at which time examination showed the swelling in the site described, the size of a large pecan. It was moderately firm, apparently movable and not attached to the muscles or tendons. The skin over the swelling was normal. Movements of the left upper extremity also were normal. Further examination showed the blood and the urine normal and the Wassermann reaction negative. The reaction to the Mantoux test was 1 plus. Roentgen examination on December 6 showed moderate swelling of the soft parts and a small, irregular shadow lying in the soft tissues anterior to the neck of the radius. The bone showed no obvious abnormalities (fig. 2).

The patient was next seen on Jan. 24, 1936, at which time the swelling of the forearm was about the size of an orange and showed definite fluctuation. A roentgenogram, which had been made on January 21, showed the small shadow previously noted occupying a position higher and farther from the bone (fig. 3).

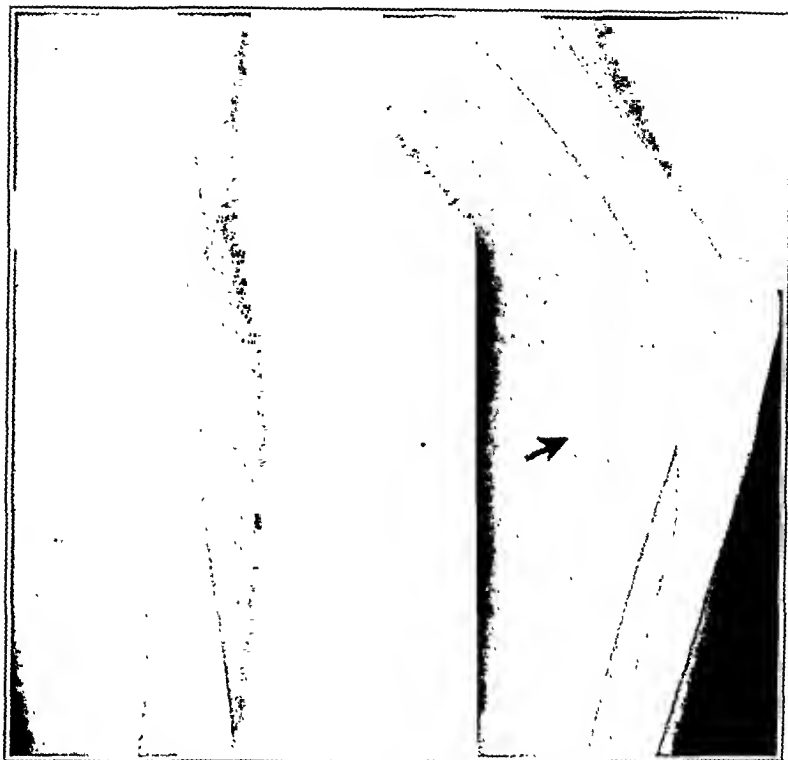


Fig. 2.—Roentgenogram made in case 2 (L. L.) on Dec. 6, 1935. The arrow points to the sequestrum.

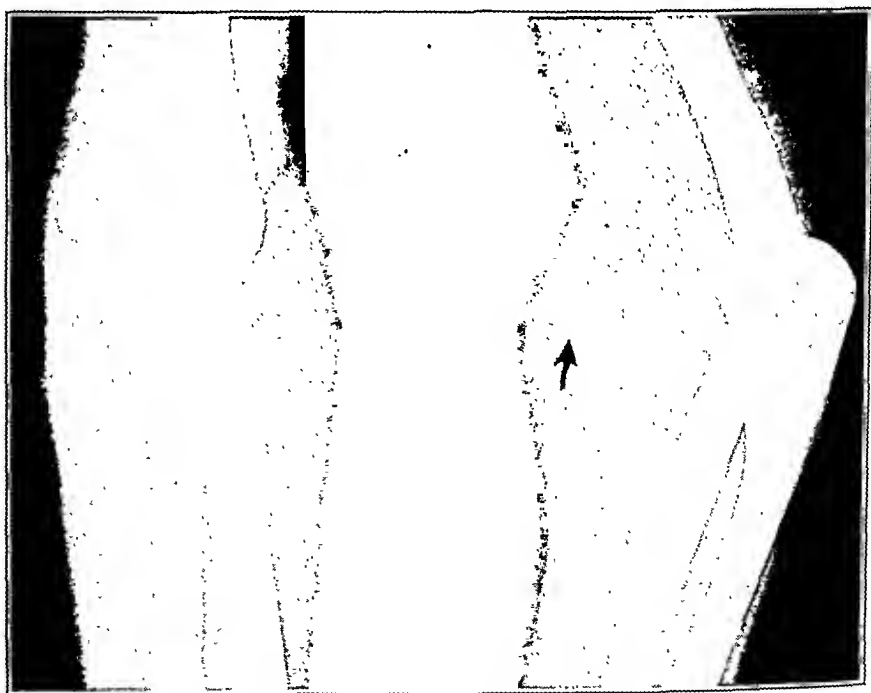


Fig. 3.—Roentgenogram made in case 2 on Jan. 21, 1936.

The patient had been able to continue her work up to this time but complained as before. At no time were there any constitutional symptoms of infection. The familial and the personal history revealed nothing of interest except a suppurative condition in the upper part of the right femur during the patient's early childhood. This condition left her with deformity and shortening of the right leg. The general examination showed no other abnormality.

In view of the similarity of this case to case 1, a diagnosis of mild, subacute infectious osteoperiostitis was made, and on January 26 the swelling was incised and drained. Abundant clear, thick, sticky yellow fluid with large and small fat globules floating on its surface, clots of fibrinous exudate and a small sequestrum were evacuated. The head and neck of the radius, palpable in the depths of the empty cavity, felt normal. No more satisfactory inspection was possible. The fibrinous clots had a striking lemon yellow tint. No definite sac was formed; the fluid appeared immediately below the deep fascia, apparently displacing the soft structures. A simple cigaret drain was inserted.

A pathologic examination was reported by Dr. George Berdez, of St. Mary's Hospital, as follows: "Macroscopically the specimen is a piece of bone, irregular in shape, measuring 1.4 by 0.5 by 0.15 cm., showing jagged edges and a rough surface. Microscopically it is seen to be formed of rather compact bony tissue, in which osteoblasts no longer stain. The edges of the bone are rough and irregular, showing signs of resorption. The tissue in the haversian canals is necrotic. A small amount of cellular connective tissue is still attached at one place to the surface of the specimen. Smears from the material show numerous polymorphonuclear cells and a few gram-positive diplococci."

Culture made from the fluid showed a pure strain of *Staph. albus*. The subsequent recovery was uneventful. The patient was apparently well in November 1936.

Clinically this case resembled case 1 in the subacute course, the accumulation of characteristic exudate, the sequestration of cortical bone and especially the roentgenographic appearance. The disease was definitely attributed to trauma, although the trauma was not to the part where the lesion occurred. The case differs from case 1 in the prompter appearance and the more rapid increase of the swelling. The fluid also, unlike that in case 1, was free in the subcutaneous tissues, contained in a large cavity without a definitely limiting wall. The condition of the bone was determined by palpation only, and the observations, therefore, are not conclusive. As in case 1, the lesion was either a primary periostitis or cortical osteitis with separation of a sequestrum, which was extruded into the exudate. The site of sequestration in the weeks prior to incision may have been covered sufficiently with granulations or scar tissue to elude the palpating finger (color plate, 16). Another striking feature of this case was the observation of free-floating fat globules on the exudate and lemon yellow clots of fibrin, obviously representing fatty degeneration. The latter observation points to the clots, rather than to the bone, as the source of the fat in the exudate. The comparatively rapid accumulation of fluid suggests a primary serous exudate, but here also the character of the initial exudate must be left

to conjecture. The cause of this infectious bony lesion may have been the suppurative disease in the upper end of the right femur in early childhood.

CASE 3.—E. P., a woman aged 41, a teacher, was first seen on Sept. 10, 1936. She had a red, ridgelike swelling of the soft parts over the root of the nail in the left middle finger. The symptoms had begun about July 4, following a severe contusion of the end of the finger. From time to time, as the swelling became tense, there would occur a discharge of a clear, jelly-like fluid from the space between the nail and the covering soft parts. After the discharge the pain and soreness would disappear, only to recur as the same peculiar jelly-like fluid again collected. Ordinary local treatment did no good. On October 10 the patient received a therapeutic dose of roentgen radiation over the finger, and one week later the symptoms had nearly disappeared. Several similar treatments were given, but when the patient was next seen, on Jan. 9, 1937, the condition was as first seen, in the preceding September. The discharge of jelly-like fluid recurred as before, the pocket filling and emptying at weekly intervals. At this time a roughened groove was noted, extending longitudinally down the middle of the nail from the point where the exudate escaped. It was about $\frac{1}{16}$ inch (0.16 cm.) in width. Roentgen examination of the finger on January 9 showed no obvious abnormalities of the bony structures of the involved phalanx.

On January 16, the swelling was incised and the soft parts lifted from the nail. Practically the whole root of the nail and the insertion of the tendon of the extensor muscle were thus exposed. The swelling at the time was, as usual, about the size of a pea and was tense, with redness of the soft parts. When the swelling was incised, a drop of the characteristic white jelly escaped. The root of the nail was seen to be loosened from its bed, and this portion of the nail was removed. A small, narrow, ridgelike area, just distal to the attachment of the tendon of the extensor muscle, was observed, covered with firm granulations. When these were removed, a small, narrow line of bare bone was noted. The wound was left open and filled with petrolatum. The jelly-like exudate yielded a pure culture of *Staph. albus*. On January 22, 2 cc. of a suspension made from the growth on gelatin was injected into the vein of the ear of a 15 week old rabbit. This experiment will be discussed later.

CASE 4.—J. H., a man aged 42, an accountant, had sustained an injury to the end of the ring finger eighteen years previously. Subsequently the finger was somewhat sore but caused only slight annoyance. Six years before the time of this record, another injury to the end of the same finger caused it to become swollen, and since then the swelling had been variable. When the swelling reached its height, the patient by squeezing evacuated a light fluid, which he stated had been "crystal clear" since the beginning of the trouble six years before. He stated that the swelling generally reached its maximum in about two weeks and that the finger was not especially sore or tender until then. After evacuation of the fluid, the discomfort in the finger eased. On Sept. 20, 1936, the swelling was incised and curetted and the wound sutured. The attacks, however, recurred within ten days after this procedure. After that time the swelling had been punctured several times. A roentgenogram of the finger made on August 26 showed no obvious abnormalities of the bony structures.

When I saw the patient, on November 5, the end of the right ring finger presented a firm red swelling in the soft parts above the nail. At its dome was a small grayish white area of hard and horny epithelium, coinciding with the

location of the sinus, which was closed at that time. The nail appeared roughened, showing marked trophic disturbance. A small V-shaped portion of the root of the nail was exposed, because of scarring and contraction following the previous incisions. Besides these abnormalities, the distal joint of the fourth finger, as well as the distal joint of the index and little fingers, of the right hand showed Heberden's nodes. Otherwise the fingers were normal in function and appearance.

Three therapeutic exposures of roentgen rays were given without apparent effect on the process. On December 11, the whole indurated swollen area was excised, and the undermined, loose part of the nail was removed. The defect in the finger was filled with petrolatum and a simple dressing applied. After removal of the indurated tissues and the sinus, the latter was found to extend to a small exposed area of bone on the dorsum of the distal phalanx. Just distal to this, the root of the nail was loosened from its bed (fig. 4 and diagram in lower right corner of color plate). Culture made from the exposed bone resulted in a growth of streptococci.

Results of a pathologic examination were reported by Dr. George Berdez: "The specimen from the top of the swelling measures 1.1 by 0.6 by 0.3 cm. The upper surface is covered with a thin skin and shows a small irregular opening of a sinus. The deeper layers of the specimen are formed of a rather compact, scarlike fibrous tissue. A smaller specimen, received separately, measures 0.3 by 0.2 by

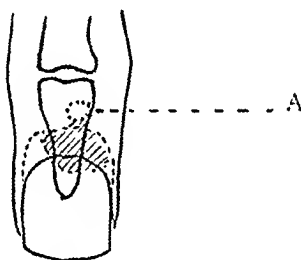


Fig. 4.—Diagram of the finger in case 4, showing the area of denuded bone at A.

0.2 cm. and is formed of red tissue of irregular shape. A third specimen is formed of a mass of fibrous tissue and measures 0.7 by 0.3 by 0.2 cm. There is also a piece of nail measuring 0.7 by 0.5 cm. and about 0.7 cm. in thickness. Microscopically the skin shows a horny layer of irregular thickness with signs of marked desquamation in places. This stratified squamous epithelial lining of the skin is fairly regular. The corium is rather fibrous and shows several small perivascular foci of cellular infiltration, with lymphocytic cells mainly. A few sweat glands, which are included in the section examined, show a slight dilatation of their lumens. The smaller specimen received separately is formed by a mass of rather fibrous connective tissue, which is infiltrated with a few scattered lymphatic cells."

On Jan. 18, 1937, the initial dressing was removed and the wound noted to be completely healed.

These 2 cases resemble closely a case reported by Edington⁴⁷ (1899), that of a woman aged 79 with an indolent swelling of three months' duration about the matrix of a finger nail. Incision produced a clear

47. Edington, G. H.: Periostitis aluminosa, *Brit. M. J.* 2:1079 (Oct. 21) 1899.

gelatinous material "precisely like that of simple ganglion." Examination of the fluid showed the presence of mucin. Microscopic examination showed degenerative flattened cells and here and there cocci arranged in chains. Edington referred to the absence of bursas in these localities and in conclusion expressed the thought that this case must be added to the bibliography of periostitis aluminosa. No other cases similar to that of Edington and the 2 here reported have been found in the literature. In case 4, the bone was bare and the root of the nail undermined, but the nail bed was intact. In case 3, a similar condition was noted, except that the small linear area of roughness was seen only after removing firm granulations. In these cases (3 and 4) there can be no thought of a previous purulent exudate changed into a gelatinous one, as the exudate reformed immediately after its evacuation. In case 3 there were noted in some of the terminal joints slight hypertrophic changes; Heberden's nodes and sharpening of the margins of the joints were seen in the roentgenogram. In case 4 these changes were somewhat more pronounced. Whether the changes or the nearness of the lesions to a tendon, if not to a joint, played a part in determining the character of the exudate is left unanswered. Careful inspection at the time of incision showed no obvious direct connection with any structures except exposed bone.

EXPERIMENT IN ANIMAL INOCULATION

A 15 week old rabbit was inoculated through the vein of an ear with 2 cc. of emulsion from a three day growth on gelatin of staphylococci obtained in case 3. The animal remained well and was killed after fifteen days. Examination showed no gross visceral lesions suggesting pyogenic infection. Both femurs with their periosteum were removed and showed no gross evidence of infection. One femur was placed in an incubator and left for thirty-six hours. The other femur was split longitudinally and the distal halves prepared in paraffin sections and stained by the Gram-Weigert method and by the use of hematoxylin and methylthionine chloride (methylene blue) and eosin. The first femur after thirty-six hours was treated similarly. Careful examination showed no cocci or demonstrable foci of infection in any part of the various specimens. Search was directed especially to the areas of the arteriovenous capillaries at the metaphyseal side of the epiphyseal cartilage.

Lexner,⁴⁸ Hobo⁴⁹ and Robertson,⁵⁰ among others, have shown that staphylococci injected intravenously into young animals produce foci of

48. Lexner, E.: (a) Die Entstehung entzündlicher Knochenherde und ihre Beziehung zu den Arterienverzweigungen der Knochen, *Arch. f. klin. Chir.* **71**:1, 1903; (b) *General Surgery*, New York, D. Appleton and Company, 1910, p. 236.

49. Hobo, T.: Zur Pathogenese der akuten haematogenen Osteomyelitis, *Acta scholae med. univ. imp. in Kioto* **4**:1, 1921.

50. Robertson, D. E.: Acute Haematogenous Osteomyelitis, *J. Bone & Joint Surg.* **9**:8 (Jan.) 1927.

infection in the spongy end of the diaphysis of a long bone, near the epiphysis. According to Lexer,^{45b}

If old attenuated cultures of the yellow or white staphylococcus are injected the animal remains sick for a short time, but recovers. During the course of the sickness several hot painful swellings develop upon one or more legs, and as the swelling of the soft tissues subsides, the thickening of the bones, which after two or three weeks present all the pathological changes of chronic suppurative osteomyelitis, as it occurs in man, becomes more distinct.

The negative result of animal inoculation in case 3 corresponds to the negative results obtained by Garré²² (1891), Scheidler¹² (1910) and Mazzini²² (1932) and denotes an organism of low virulence. The results obtained by Dor²² (1895) and Stropeni¹⁶ (1933) from animal inoculation likewise point to an attenuated organism.

COMMENT

A review of the foregoing material shows that the lesions in the recorded cases were chiefly (93 per cent in this series) periosteal or cortical in origin. In their tendency to involve the superficial bony structures, in their clinical course and in their characteristic exudate, they differ from those of ordinary osseous infection. Only in their subacute course do they resemble the rarer forms of attenuated infection associated with the names of Brodie and Garré. For this reason, I do not hesitate, in the subtitle of this paper, to associate the name of Ollier with this form of chronic bony infection. The cases of Legiehn (Mikulicz) (1889), Beckenkamp (1890), Lexer¹⁹ (1898), Deutschländer²² (1905) and Garré²² (color plate, 33, 34 and 35) represent lesions which were probably cortical from the beginning (osteomyelitis). The case of Deutschländer was one of direct primary infection of the marrow cavity following an open fracture of a bone. In the remaining cases of this group the infection spread locally from a primary focus in the spongy part of the broadened metaphysis (subepiphysial) of bone secondary to generalized bacteremia. This process is described by Lexer,⁴⁵ Hobo⁴⁹ and Robertson.⁵⁰ Of special interest are the cases of osteomyelitis aluminosa reported by Ehrlich⁵⁰ and by Schlange,⁹ the latter described in connection with 3 others, which Schlange designated as instances of "nonsuppurative osteomyelitis" of the femur. Schlange stated a preference for the term nonsuppurative rather than aluminosa. A careful study of his cases (color plate, 14, 23 and 32) suggests that they involved a primary cortical and not an osteomyelitic lesion.

In Ehrlich's case (color plate, 37) a cyst of the distal end of the tibia occurred in a man aged 23, after an acute onset, with high fever, pain, redness and swelling. There was a tumor-like swelling of the bone, which on incision yielded a stringy, synovia-like fluid. The cavity was lined with thick, firm granulations, and under

these was a smooth bony wall. Bacterial examination showed on culture pyogenic staphylococci. The patient recovered.

In Schlange's case of a boy aged 14, there had occurred a contusion of the tibia one and one-half years previously, followed by tenderness and swelling with fever and malaise. This was followed by a gradual recovery, but some fusiform swelling of the upper third of the tibia remained. At the time of surgical exploration, the cortex was thin and parchment-like and the cavity ovoid, filled with brown serous fluid and lined with soft dark brown tissue. The underlying bone was soft and porous. The fluid contained a few red and white blood cells and occasional fat cells and was albuminous. In the fluid were a few clumps of brown-red tissue, which was poor in cells and contained giant cells. The osseous specimens were lost, and no further microscopic or bacteriologic examination was made. Recovery was uneventful.

A considerable degree of speculation continues as to the causation of many so-called simple bony cysts which have been reported, such as those described by Schlange. Osteitis albuminosa is included as a cause in most classifications and discussions of bone cyst and fibrocystic disease of bone. Beck,⁵¹ Tietze,⁵² Silver,⁵³ Felten and Stoltzenberg,⁵⁴ von Bergmann,⁵⁵ Bolognesi,⁵⁶ Meyerding⁵⁷ and Ashhurst, Bromer and White,⁵⁸ among others, concerned themselves with this problem. In occasional cases reported by some of them the infectious character is evident, as in Ehrich's case, and in others it may be strongly suspected. Phemister and Gordon⁵⁹ stated the belief that infection is a major cause of "solitary bone cysts" and that more careful bacteriologic studies may prove infectious many conditions now classified otherwise. It is not the purpose here to enter into a discussion of cysts, benign or malignant, of bone. It is intended rather to point out the part which attenuated bacterial infections may play in their causation. Exclusion of these cases of osteitis albuminosa from general discussions of cystic changes in bone would unburden to some extent the literature dealing with "genuine bony cysts" (Tietze⁵²) and other cystic diseases of bone.

51. Beck, C.: Osseous Cysts of the Tibia, *Am. J. M. Sc.* **121**:667, 1901.

52. Tietze, A.: Die Knochenzysten, *Ergebn. d. Chir. u. Orthop.* **2**:32, 1911.

53. Silver, D.: The So-Called Benign Cyst of the Bones, *Am. J. Orthop. Surg.* **9**:563 (May) 1912.

54. Felten, R., and Stoltzenberg, F.: Traumatische solitäre Knochenzysten, *Ztschr. f. orthop. Chir.* **30**:430, 1912.

55. von Bergmann, G.: Zur Kasuistik von Cysten in den langen Röhrenknochen, *Deutsche Ztschr. f. Chir.* **124**:1 (Sept.) 1913.

56. Bolognesi, J.: Ueber die Pathogenese der sogenannten Knochenzysten, *Deutsche Ztschr. f. Chir.* **131**:382 (Sept.) 1914.

57. Meyerding, H.: Cystic and Fibrocystic Disease of Long Bones, *Am. J. Orthop. Surg.* **16**:253 (Sept.) 1918.

58. Ashhurst, A.; Bromer, R., and White, C.: Cystic Disease of the Bones, *Arch. Surg.* **6**:661 (May) 1923.

59. Phemister, D. B., and Gordon, J. E.: The Etiology of Solitary Bone Cyst, *J. A. M. A.* **87**:1429 (Oct. 30) 1926.

SUMMARY

A form of osteoperiostitis first noted by Ollier is described. It is an infection caused by the pathogenic organisms usual in ordinary forms of superficial and deep osseous infection, but of low virulence. The lesions in this form are usually superficial and localized but occasionally of deeper origin.

Trauma, though it plays a part in causing this form of osseous infection, is not to be regarded as the primary or sole etiologic factor. Inability to demonstrate the presence of micro-organisms in the lesions does not establish their absence.

The indolent character of the process and the absence of the usual signs of infection in cases of osteoperiostitis aluminosa may cause diagnostic difficulties. Tuberculosis, when it is in question, can usually be recognized by roentgenologic study, by examination of tissue or by animal inoculation. Malignant growths have at times been simulated by the history of gradual onset and progression and by roentgenographic characteristics. Confusion in diagnosis has occurred in cases of osteoperiostitis aluminosa with accumulations of synovia-like exudate when these accumulations were located in regions ordinarily the seat of ganglions and cysts. Aspiration and roentgen examination may clarify the picture.

The lesions are mild and benign. Simple incision with adequate drainage and removal of sequestrums, whether or not the cystlike structures are removed, suffices usually for recovery within a short time.

The centrally located lesion of osteomyelitis aluminosa should be distinguished from the "genuine bony cyst."

TIC DOULOUREUX

PARTIAL SECTION OF THE ROOT OF THE FIFTH CRANIAL NERVE; A
COMPARISON OF THE SUBTEMPORAL AND CEREBELLAR APPROACHES
FROM SURGICAL AND PHYSIOLOGIC STANDPOINTS

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The development of a surgical cure for tic douloureux presents one of the most brilliant chapters in the history of surgery of the nervous system and indicates step by step how surely and definitely progress may be made.¹

At the present time there are two cleancut operative procedures by which the sensory root of the fifth nerve may be sectioned partially or entirely, producing a cure of the hideous malady and entailing a negligible mortality in experienced hands.

There is some controversy concerning the relative merits of the two procedures, and I felt the need of a comparative study by one person.

Many interesting and important problems arise, both theoretic and practical, when an incomplete section of the fifth root is considered. I wish to suggest possible explanations for certain paradoxes and discrepancies in results and to report that my experiences have confirmed the fact that "tic douloureux," at least that involving the second and third branch distribution, can be cured surgically with losses in all modalities of sensation so trivial as to be undetected by the patient.

This great stride in the perfection of an ideal in surgery adds the final achievement to the triumphs of those persevering pioneers who directed a courageous and relentless attack on a field no larger than an inch in diameter for over forty years.

From the Department of Surgery of the College of Medicine, State University of Iowa.

1. (a) Frazier, C. H.: Radical Operations for Major Trigeminal Neuralgia, J. A. M. A. **96**:913-916 (March 21) 1931. (b) Dandy, W. E.: Operation for the Cure of Tic Douloureux: Partial Section of the Sensory Root at the Pons, Arch. Surg. **18**:687-734 (Feb.) 1929. (c) Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1932, vol. 12.

COMPARISON OF THE APPROACHES FROM A
SURGICAL STANDPOINT

SUBTEMPORAL APPROACH

The subtemporal approach to the root of the fifth cranial nerve is almost universally used. The essentials in operative technic have been worked out in detail and to a highly successful end by Frazier,¹ Adson,² Stookey³ and others.

A linear incision is made in the temporal region beginning at a point directly above and about 4 cm. from the superior margin of the pinna and is carried forward to the zygomatic process about a finger's breadth anterior to the external auditory meatus. The line of intersection of a transverse and a coronal plane passed through the latter point will usually pass through the foramen spinosum. In other words, the trunk of the middle meningeal artery, which is the most important point in the procedure, will be straight in from a point a finger's breadth anterior to the external auditory meatus. The wound is spread by a suitable self-retaining retractor and a bony defect about 5 cm. in diameter is prepared. The dura is gently and slowly elevated to the foramen spinosum and the meningeal artery is dispensed with either by ligating it or by plugging the foramen and cutting. The mandibular branch of the fifth nerve as it disappears into the foramen ovale is regularly found just anterior and mesial to the foramen spinosum. After carefully loosening the point of adherence of the dura to the third branch, the former can be stripped from the lateral face of the semilunar ganglion by pushing it firmly upward with a small solid cotton ball fixed in a hemostat. The pulsating arachnoid membrane which is reflected over the posterior aspect of the ganglion and root comes into view. When the arachnoid membrane is incised the fan-shaped sensory root is well exposed. The motor root is a single large distinct filament; it is concealed from view, since it courses mesially to the sensory root and superoinferiorly. The inferior filaments of the sensory root are sectioned as extensively as the occasion may demand.

CEREBELLAR APPROACH

The cerebellar approach was developed by Dandy⁴ and has been almost exclusively used by him. He has listed the following advantages of the approach: (1) There is never corneal disturbance as the result of the operation; (2) there is never injury of the motor branch; (3)

2. Adson, A. W.: The Diagnosis and Surgical Treatment of Trigeminal Neuralgia, *Ann. Otol., Rhin. & Laryng.* **35**:601-631 (Sept.) 1926.

3. Stookey, B.: Differential Section of the Trigeminal Root in the Surgical Treatment of Trigeminal Neuralgia, *Ann. Surg.* **87**:172-178 (Feb.) 1928.

4. Dandy, W. E.: The Treatment of Trigeminal Neuralgia by the Cerebellar Route, *Ann. Surg.* **96**:787-795 (Oct.) 1932.

I have now designed a guillotine knife the shaft of which is a lumbar puncture needle (fig. 2). The hooked end is placed to the desired depth under the root, and the blade is driven home, making a clean, accurate cut with no undue injury to the nerve. Stereoscopic vision is not necessary and the size of the exposure may be minimal.⁵

I have noted the possibility and the probability of injuring the root at operation more than was intended. I have had 2 cases in which this occurred. The reason for it is that the tender root will often be avulsed at the pons more easily than it will be divided. (I have confirmed this a number of times at the necropsy table.) It may still occur even though one uses a sharp hook knife, so that if one attempts to section half the nerve root with a hook knife one may cause avulsion of the entire root and not be aware of it. At any rate it is certainly possible to cause a greater injury than was intended. Particularly if the root is sectioned by the subtemporal route there will be less chance of one's being cognizant of the total injury than if the root is sectioned at the pons. I feel confident that this may explain a great discrepancy that has existed in the findings after a supposed partial section. Hence the greater need for instruments that will obviate such an outcome.

Another important part of the equipment for this operation is the means of illumination. It is absolutely necessary for the operator to see well what he is doing. Lighted retractors which are on the market at present are entirely impractical. They occupy too much space; moreover, should fluid and blood obscure the light they would leave the operator without illumination at the time he needs it most. A head lamp is the preferable source of illumination. Having failed to find a head lamp satisfactory for this purpose, I set out to make one. The result has proved so useful that I feel it worth while to incorporate a description of the lamp here.

The essential requirement of such a lamp is that it throw a small, bright spotlight into the operative field. Low voltage lamps are superior. A full size, 2 cell, adjustable focus flashlight is dismantled and the head is cut off on a bevel that will give the proper tilt of the reflector (fig. 3).

One connector is present in the head, but a second must be soldered into the head to provide contact with the center connector of the bulb. Wire leads are soldered to the connectors, and the head is backed by a piece of stiff cardboard or other suitable material. Any form of celluloid-acetone glue will suffice to fix the piece. A 9 volt flashlight bulb is ideal, and the reflector is adjusted to make the spotlight satisfactory.

5. This instrument was milled by Mr. A. P. Freund, Mechanician, Pharmacology and Physiology Shop, State University of Iowa. Duplicates may be obtained from him.

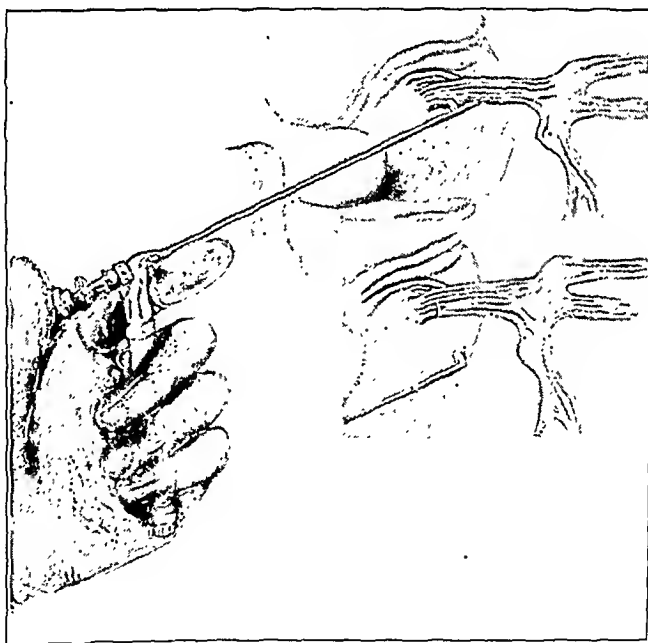
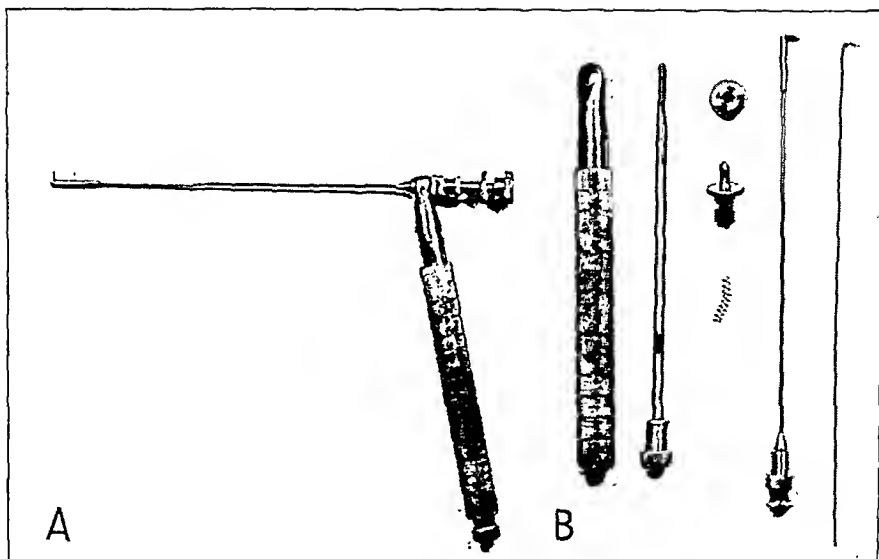


Fig. 2.—Guillotine knife. *A*, knife assembled. The tiny blade moves freely into a slotted guard when the thumb button is pressed. The blade returns by spring action. The blade was designed so that its length would be equal to only half the width of the average sensory root at the pons. *B*, parts of the instrument. Left to right: handle; set screw by means of which the blade shaft may be rotated at any angle to the handle; thumb screw which fixes the blade rod; blade rod guide; spring; blade shaft with terminal slotted guard (made from lumbar puncture needle); blade, made from piano wire. This may be easily and inexpensively renewed from time to time if necessary). The instrument should be sterilized in the autoclave. The drawing below illustrates the use of the instrument. The insert shows the section completed.

This light will remain concentrated at varying distances. A simple arrangement is to cover the bulb socket with a small section of snug-fitting rubber tubing of such a size that the reflector may be snugly twisted over it. The reflector may then be adjusted properly and glued to the rubber sleeve.

If the source of current is the ordinary 110 volt circuit, a 9 volt transformer must be interposed. I found that the 9 volt transformers supplied with toy electric trains are satisfactory and inexpensive. They may be obtained separately. There is no need of covering the reflector. If it tarnishes it may be polished, or the whole piece may be preserved in a case when not in use.

The lamp may be fastened to wide elastic tape made to fit the operator's head. The wire goes over the head and is fastened to the elastic

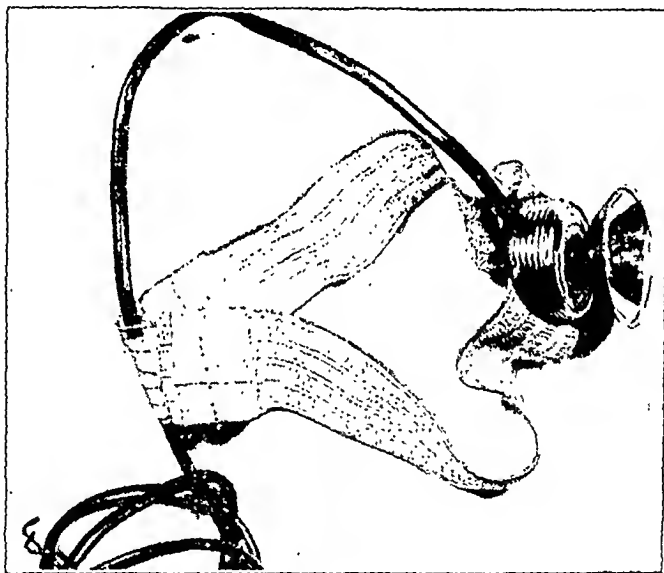


Fig. 3.—A useful head lamp, providing the proper illumination for operating through small deep exposures. The lamp is described in the text.

in the back. After the head piece is glued to the tape a thread is placed through the two holes in the head piece and through the backing and the tape, so as to provide additional security against the lamp's falling from the tape.

The finished product is small and light, does not become hot, is easily applied during the operation and is inexpensive. It fulfils exactly the needs in illumination for this procedure.

ADVANTAGES AND DISADVANTAGES OF THE TWO METHODS OF EXPOSURE FROM A SURGICAL STANDPOINT

The incision through skin, muscle and bone is quicker, easier and attended with less bleeding in the subtemporal exposure. Facial palsy

occasionally occurs with the subtemporal exposure and has been attributed to an indirect injury of the geniculate ganglion through an injury to the petrosal nerves. When this has occurred in my cases it has disappeared later. I have at times felt it might be due to injury or section of the peripheral branches of the seventh nerve, but its general absence after decompressions made through similar incisions obviates such a possibility.

In respect to the cerebellar approach, although with a reasonable amount of skill one should be able to manipulate without injuring the seventh nerve, it cannot be gainsaid that this nerve is always in a vulnerable spot. If it tears apart, the injury is permanent and irreparable, save for spinofacial anastomosis.

The subtemporal approach has the advantage of being largely but not entirely extradural.

I have found bleeding to be more troublesome with the subtemporal approach than with the cerebellar approach. Stripping the dura may be attended in certain cases by venous oozing that requires much time and patience to control, particularly since it is often impossible to find the source of the bleeding. With the cerebellar approach, provided the petrosal veins are properly cared for (and I have encountered no difficulty at this point) the intracranial portion of this operation may be entirely bloodless. On the whole, the middle meningeal artery and the petrosal veins are about equally matched as hazards in the two approaches.

I have had no difficulty in differentiating and preserving the motor root in the temporal approach, although it is necessary at times to manipulate it in separating it from the sensory filaments. No manipulation is necessary in the cerebellar approach.

Occasionally a thin, adherent dura which repeatedly tears constitutes a distinct disadvantage in the temporal exposure, and if the dura tears at the ganglion and is unusually adherent to it the operator may be completely defeated. The tendency in such a situation is not to give up until the operator is exhausted and perhaps an unnecessary amount of damage has been done to the patient. Such an ultimate defeat is not so likely in a well directed cerebellar approach. It may be that previous injections of alcohol cause the dura to become more firmly adherent to the ganglion.

In the cerebellar exposure the occipital nerves to the scalp are sectioned, and there results a degree of numbness in their distribution. This is a criticism of the cerebellar approach, but a minor one, because it is only minimally disturbing to the patient and with proper anatomic closure is not permanent.

Dandy⁴ states that he does not carry his incision far enough to include the great occipital nerve.

The first incisions made by me, such as that shown in figure 9, were more extensive than was necessary. The incision has been reduced to the size illustrated in figure 11. This incision easily avoids the great occipital nerve and it has proved no more difficult to reach the cerebellar cistern and complete the operation with this incision than through a larger exposure.

At the termination of a subtemporal approach the degree of dural and osseous oozing will often, though not always, make it advisable, as Adson has maintained, to leave a gauze pack planted against the ganglion. The subsequent removal of this pack is not altogether pleasant for either the surgeon or the patient, and the use of drainage material is always precarious in surgical operation on the brain. I have never seen any indication for employing drainage material or packs in making the cerebellar approach.

In conclusion, speaking from a surgical standpoint, I feel that the odds are in favor of the cerebellar approach as being a finer, more bloodless and more dependable operation. It requires, however, a greater measure of technical skill and experience in the cerebellar fossa and decidedly more care.

ETIOLOGY OF TIC DOULOUREUX

With respect to the cause of tic douloureux, it may be said that any impression at the present time is purely hypothetical. The locus operandi has variously been placed at the receptor of the sensory nerve, the branches, the ganglion, the root, the bulbar contingent and even the thalamus. No incontrovertible evidence has been brought forth in any case, and objective pathologic changes have been uniformly absent.⁶ One clinical fact seems well established, however, which is that when the end organ is destroyed or anesthetized, particularly in the region of the trigger zones, the crises cease to occur, and when the function of the end organ is restored the painful crises reappear. In this light I feel it worth while to recall the experiments of Davis and Pollock.⁷ When the superior cervical ganglion is stimulated in the cat under the influence of bulbo-capnine, the animal exhibits definite symptoms of severe pain in the

6. W. E. Dandy (Concerning the Cause of Trigeminal Neuralgia, *Am. J. Surg.* **24**:447-455 [May] 1934) has reported a high incidence (60 per cent) of gross pathologic changes uncovered by the cerebellar exposure which he felt were of etiologic importance. Five and six-tenths per cent of the lesions encountered were tumors of the cerebellopontile angle.

7. Davis, L., and Pollock, L. J.: The Role of the Sympathetic Nervous System in the Production of Pain in the Head, *Arch. Neurol. & Psychiat.* **27**: 282-293 (Feb.) 1932.

head. The pain lasts only during the period of stimulation and occurs whether the proximal cervical chain is intact or not. Section of the anterior and posterior spinal roots from the first to the twelfth thoracic does not abolish the phenomenon, but section of the fifth root in addition does abolish it. Davis and Pollock⁷ concluded that something was taking place at the sympathetic terminals that was relayed through the afferent fibers of the fifth nerve and interpreted as pain. Stimulation of the cervical chain proximal to the superior cervical ganglion had the effect only of dilating the ipsilateral pupil and causing movements of the nictitating membrane. With the cooperation of Dr. Tracy Putnam I had the opportunity at the Boston City Hospital of confirming these results so far as stimulation of the superior cervical ganglion is concerned, but no sensory roots were sectioned. To my knowledge there is no evidence to show whether this pain is instigated at the receptor or at the ganglion of the fifth nerve.

The abolition of visceral pain by section of the abdominal sympathetic nerves has been accomplished by Archibald⁸ and Scrimger.⁹

In short, it appears to be established that there do exist afferent visceral fibers that mediate pain, and it is possible that they retain their identity to the thalamus.

It is possible that the pain of tic douloureux is mediated by similar fibers coursing along with but anatomically distinct from the cerebro-spinal fibers of the fifth nerve. This would help to explain the paradoxical results obtained in the cure of tic douloureux by partial section of the fifth root. Such a hypothesis is strongly suggested because the paroxysms are unlike pain which is known to be mediated by the cerebro-spinal afferent nerve fibers and do closely simulate the excruciating visceral paroxysms, such as gallbladder and ureteral colic, and, if the comparison is permissible, tabetic crises. Moreover, the exciting factors, such as stroking the skin and cold drafts, are not stimuli ordinarily associated with the initiation of pain which is transmitted by cerebro-spinal afferent fibers.

It is not to be implied that efferent cervical sympathetic nerve fibers are responsible for tic douloureux, but these facts do suggest that the pain of tic douloureux and the pain shown by the animals mentioned may be mediated by afferent sympathetic nerves through the fifth nerve.

8. Archibald, E.: Effect of Sympathectomy upon the Pain of Organic Disease of the Arteries of the Lower Limbs and for Obscure Abdominal Pain, *Ann. Surg.* **88**:499-509 (Sept.) 1928.

9. Scrimger, F. A. C.: On the Possibility of Relieving Abdominal Pain by Section of Sympathetic Rami Communicantes, *Canad. M. A. J.* **21**:184-189 (Aug.) 1929.

RESULTS OF PARTIAL SECTION OF THE ROOT OF THE FIFTH NERVE AND THEIR THEORETIC EXPLANATION

There has been considerable controversy concerning the all-important arrangement of fibers in the root of the fifth nerve and their relation to those of the peripheral branches. On clinical grounds there seems to be a consensus that some topographic relation is maintained in the ganglion and the root so that the upper, middle and lower thirds of the root correspond roughly with the first, second and third peripheral divisions of the nerve.¹⁰ Opposition to this concept has been on anatomic grounds.¹¹

Davis and Haven¹² studied macroscopically and microscopically the root fibers and the bulbar fibers, after degeneration, from various sections in the cat. In this animal they found the root to be rotated so that the ophthalmic fibers, which are superior just proximal to the ganglion, become inferior as the root enters the pons. Hence a section of the superior half of the nerve just proximal to the ganglion gives the same degeneration picture in the spinal root as does a section of the inferior half of the root as it enters the pons. They stated that the root is rotated in a like manner in man. Clinical results, however, do not bear this out.¹³ They found in the degeneration experiments that the fibers in the spinal root of the cat are so disposed that those from the ophthalmic nerve are ventral and those from the mandibular nerve are dorsal. In either case degeneration is evident throughout the entire length of the spinal root. This indicates that the topographic relationship in the root maintains itself even in the brain stem. Spiller¹⁴ made these observations as early as 1901, and Bregman¹⁵ in 1892, with rabbits. The five authors were in agreement on the findings.

10. Frazier, C. H.: Subtotal Resection of Sensory Root for Relief of Major Trigeminal Neuralgia, *Arch. Neurol. & Psychiat.* **13**:378-384 (March) 1925. Frazier, C. H., and Whitehead, E.: Morphology of the Gasserian Ganglion, *Brain* **48**:458-475 (Dec.) 1925. Stookey.³

11. Van Nouhuys, F.: The Anatomy of the Gasserian Ganglion: Its Relation to Tic Douloureux, *Arch. Surg.* **24**:451-457 (March) 1932.

12. Davis, L., and Haven, H. A.: Surgical Anatomy of the Sensory Root of the Trigeminal Nerve, *Arch. Neurol. & Psychiat.* **29**:1-15 (Jan.) 1933.

13. My observations of the nerve root at the necropsy table have convinced me that the rotation of the root from ganglion to pons is about 20 to 30 degrees but certainly not of the magnitude of 180 degrees.

14. Spiller, W. G., and Frazier, C. H.: The Division of the Sensory Root of the Trigeminal for the Relief of Tic Douloureux: An Experimental, Pathological and Clinical Study, with a Preliminary Report of One Surgically Successful Case, *Univ. Pennsylvania M. Bull.* **14**:341 (Dec.) 1901; *Philadelphia M. J.* **8**:1039, 1901.

15. Bregman, E.: Ueber experimentelle aufsteigende Degeneration motorischer und sensibler Hirnnerven, *Arch. a. d. Inst. f. Anat. u. Physiol.* **1**:73-97, 1892.

Davis and Haven¹² after experiments in teasing the human nerve root pointed out a liberal anastomosis between the macroscopic filaments. Microscopically they were unable to find a topographic segregation of small and large fibers in the root. Spiller,¹⁴ however, logically pointed out that physiologic implications may not always be drawn accurately from anatomic findings.

On clinical grounds the following observations would seem incontrovertible:

1. As one sections the root from below upward, whether at the pons or at the ganglion, the loss of sensation progresses from the lowermost distribution in the face upward and from the midsagittal plane laterally. (Observations made by the department of neurology and by myself after partial sections of the fifth root have not exhibited losses in sensation with as cleancut boundaries as have been indicated in Frazier's reports.¹⁵ In fact, when losses in various modalities of sensation could be demonstrated it has been my impression that they conform more to a segmental or nuclear distribution than to a peripheral branch distribution.)

Although degeneration experiments have demonstrated the ventro-dorsal disposition of fibers in the spinal root, no evidence, save in cases of syringobulbia¹⁶ has been forthcoming concerning the disposition in the long axis of the spinal root. Spiller has expressed the view that the descending spinal root represents pain and temperature sensation and that there is evidence to show that the sensations of pain, heat and cold may be to some extent anatomically segregated, as is the case in the spinothalamic tracts. It appears that sensory distribution from the midsagittal plane of the face laterally is represented in the long axis of the spinal root and that the fibers representing the most lateral distribution in the face extend farthest caudad in the spinal root.

It thus appears that one of the differences in the results obtained by cutting a peripheral branch and by partially cutting the nerve root is that in the latter a combined branch and segmental loss obtains.

2. Section of the inferior half of the root may eliminate the pain crises of tic douloureux, at least in the second and third branches, and loss of any modality of sensation in the face may be so insignificant as to be unnoticeable by the patient and to require most careful examination for its detection. If the loss is detectable, it involves sensation to pain more than to light touch and is diffusely distributed over an area rather than bounded by cleancut borders.

I have verified this statement so far as the cerebellar approach is concerned, but I am not wholly prepared to make the same statement for

16. (a) Grinker, R. R.: *Neurology*, Springfield, Ill., Charles C. Thomas, Publisher, 1934, p. 330. (b) Jelliffe, S. E., and White, W. A.: *Diseases of the Nervous System*, ed. 4, Philadelphia, Lea & Febiger, 1923, plate X.

the subtemporal approach. The partial sections made by the subtemporal approach have been extended much farther than half the length of the nerve. In fact, until now only one macroscopic filament has been left in the upper aspect of the root. This was done through fear of an insufficient operation. The remaining fasciculus proved adequate to supply the ophthalmic distribution and corneal sensation, with no detectable loss in that field.

I should like to suggest the following explanation to account for the incommensurate retention of sensation after a partial section of the sensory root. It should be remembered that the fifth nerve is a single nerve which peripherally has been split three ways but that this peripheral division should in no way destroy the possibilities of overlap that characterize the sensory domain. It is not unlikely that the plan of innervation is that indicated in figure 4 *A*. The uppermost neurons (*A*) send dendrites largely to the ophthalmic distribution (*O*). The next lower neurons (*B*) innervate the ophthalmic and maxillary regions. The middle neurons (*C*) send dendrites to all three divisions, and the still lower neurons (*D*), to the maxillary and mandibular regions. The lowermost neurons (*E*) largely innervate the mandibular region.

If only the *E* fibers are sectioned, little loss will be expected even in the mandibular division. If *D* and *E* (probably representing the lower third of the root) are sectioned, there will still not be a total loss even in the mandibular region. The diagram can thus be worked out for various sections and is the simplest possible diagrammatic representation of the scheme of innervation. It is likely that the three way distribution of the dendrites is far more extensive for each neuron than is indicated in the diagram. This plan of overlap would adequately explain how the nervous system might conserve the number of axons necessary to innervate a broad surface of skin. This will also explain the phenomena of referred sensations demonstrated in case 1 in the following manner: First, consider the simplest possible plan shown diagrammatically in figure 4 *B*, of three neurons each having independent dendrites and receptors as well as receptors in close contiguity with their fellows. If receptor X_1 is stimulated, the stimulus will be transmitted only by the axon *X*. If the locus of stimulation is a point where X_2 and Y_1 are contiguous,, the stimulus will be transmitted by axons *X* and *Y*. If at Y_2 , *Y* alone will carry the impulse. In this manner, such a plan as shown in the diagram provides five different combinations or patterns of stimulus transmission, or combinations equal to $2^N - 1$, when *N* is the number of neurons. This may be called a combination of first order.

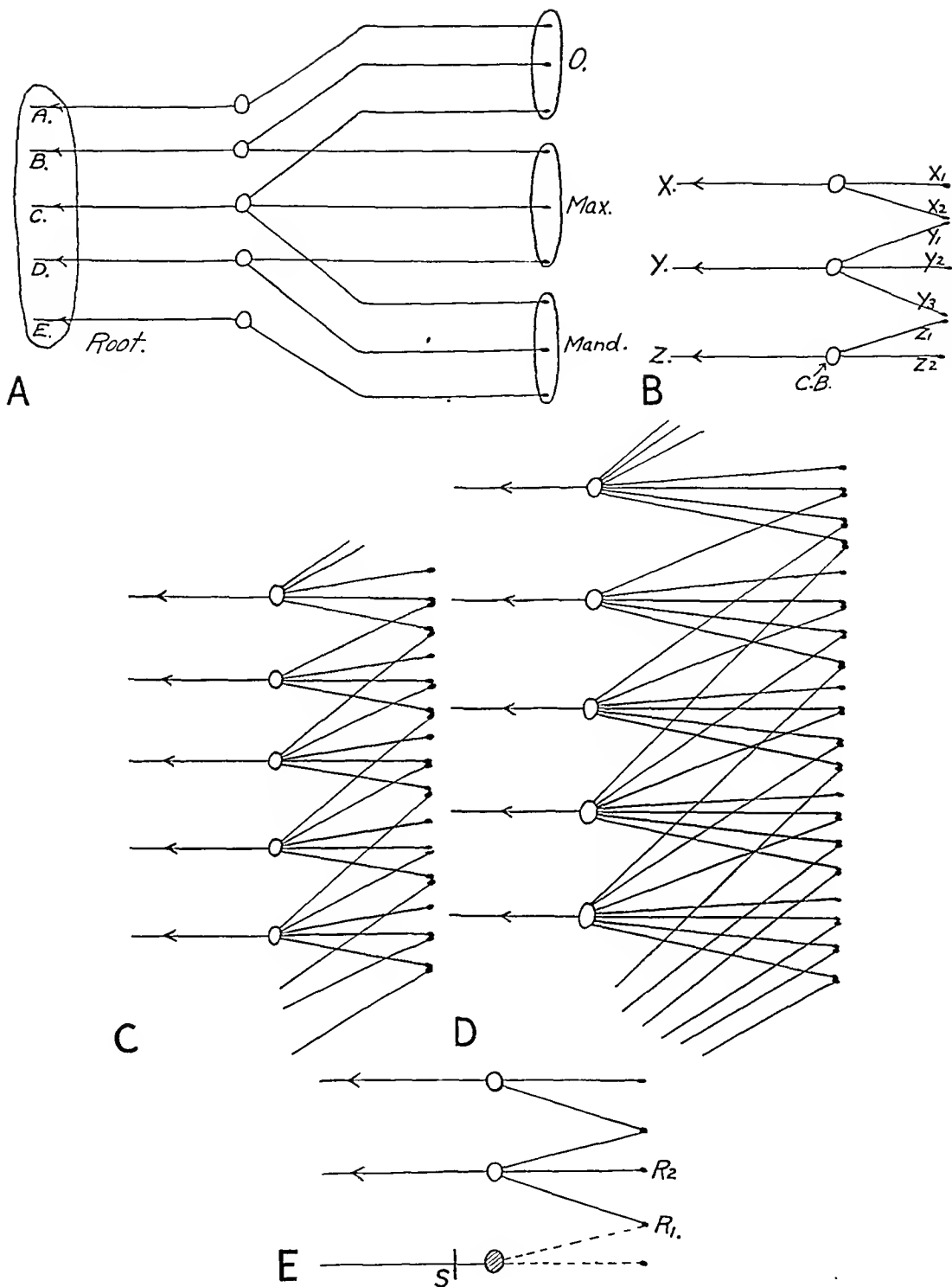


Fig. 4.—*A*, diagrammatic representation of a hypothetical plan of overlap in the sensory fifth nerve. *A-E*, axons; *O*, *max.*, *mand.*, ophthalmic, maxillary and mandibular branches of the fifth nerve (see explanation in text). *B*, diagrammatic representation of a hypothetical plan of sensory innervation of the skin, illustrating the simplest plan of neuron combinations. *X*, *Y* and *Z*, axons; *X*₁, free receptor for *X*; *X*₂ and *Y*₁, contiguous receptors or single receptor for *X* and *Y*; *Y*₂, free receptor for *Y*, etc.; *C. B.*, body of cell. The possible axon pattern combinations in this diagram equals $2N-1$, *N* being the number of neurons. (See explanation in text.) *C*, diagram illustrating a combination of each neuron with four of its fellows, a plan of second order. The number of axon pattern combinations possible in this diagram equal $3N-3$. *D*, diagram illustrating a combination of each neuron with six of its fellows, a plan of third order. The number of possible axon combinations in this diagram equals $4N-6$. *E*, diagram of the simplest plan to illustrate the possible mechanism of the phenomenon of referred sensation. *S*, section of axon; *R*₁, disassociated receptor; *R*₂, free receptor of middle neuron. (See text for explanation.) This concept will adequately account for the phenomena of spread and hy-

If one assumes a more complex arrangement, such as that shown in figure 4 *C*, in which each neuron has contiguous receptors with four of its fellows, the possible axon combinations will be $3^N - 3$, a combination of second order.

If, as in figure 4 *D*, each neuron has contiguous receptors with six of its fellows, the possible combinations will be $4^N - 6$, a combination of third order.

That is, 100 axons could supply about 400 skin loci, each of which could be discriminated from the other, *provided* one accepts the proposition that such axonal patterns of afferent stimuli could provide a mechanism of integration in terms of localization. It seems to me that some such plan must obtain to account anatomically for the evident conservation of axons in the nerve roots and in the spinal cord.

So far as the receptors are concerned, it is not too imaginative to assume that the dendrites of several neurons take origin from a single receptor rather than from contiguous receptors as indicated in the diagram.

The phenomenon of referred sensation, as exhibited in case 1, may then be explained as follows:

If, as in figure 4 *E* (the simplest possible diagram), an axon is severed at *S*, all the dendrites indicated by dotted lines cease to function, and hence, with the standard pattern disrupted, if a stimulus is applied to receptor R_1 it can only be interpreted as having been applied to the free receptor, R_2 . Hence, the distance from the actual stimulus to the point of reference may give a rough indication of the magnitude of the territory innervated by a single neuron.

WHY "TIC" SHOULD BE ELIMINATED WHEN SENSATION IN GENERAL HAS BEEN SO LITTLE DISTURBED

Two possible reasons for the elimination of the "tic" are suggested: First, one may be dealing with a pain which is mediated by afferent sympathetic nerves, as pointed out in the section on etiologic considerations, and it may be that the involved fibers are cut in the procedure. Second, the trigger zones may be the sole regions of excitation of the pain. Indeed, if such regions are locally anesthetized the pain is abolished until the anesthesia disappears.

The trigger zones are almost always situated in the gums, in the buccal mucosa or about the lips or the side of the nose; that is, they are usually located within the innermost segment of the distribution of the fifth nerve.

When the lowermost fibers of the root are sectioned, it is this segment that is most involved, particularly with respect to pain sensation, and the denervation may be just sufficient to abolish the abnormal reaction of the trigger zones.

COMPARISON OF THE TWO APPROACHES FROM A
PHYSIOLOGIC STANDPOINT

Corneal Ulcer.—I have been spared the occurrence of corneal ulceration in all my cases of partial section when corneal sensation has been preserved, whether the approach was subtemporal or cerebellar. A corneal ulcer has developed in 1 case for each exposure when the division of the sensory root was complete and corneal sensation was lost. It is felt that loss in corneal innervation is the important feature, regardless of the approach. An early lesion is probably on a trophic basis, as is herpes of the skin, though the cornea may subsequently be inadvertently injured because of the anesthesia.

REPORT OF CASES¹⁷

SUBTEMPORAL EXPOSURES

CASE 1.—B. W., a white woman aged 50, was referred to me by Dr. George D. Callahan, of Iowa City, in May 1936. She dated the onset of her attacks to 1920, after the extraction of an abscessed tooth. The pain was sharp and stabbing and lasted from three to four seconds. It began anterior to the right ear and radiated to the mouth. In 1928 an attempted operation by the subtemporal exposure was unsuccessful. After the operation she noticed that part of the right cheek was numb. There was a transient palsy of the sixth nerve on the right side. In less than a month the painful seizures had returned.

On this admission to the hospital, she stated that the attacks had become so frequent and severe that she had been in constant agony and unable to sleep. The pain started in the right malar region and radiated to the right buccal angle. The right half of the tongue was severely involved and appeared to be a trigger zone. Excitement, worry, nervousness, a draft of air, chewing and swallowing were exciting factors. On examination a small portion of the anterior part of the right cheek revealed about a 20 per cent loss of sensation to light touch and to pain. By a subtemporal approach on the right side the sensory root of the fifth nerve was exposed, and all its fibers were sectioned with the exception of the most superior fasciculus. The motor root was identified and spared. The wound healed uneventfully, and pain has remained absent to the present time (ten months).

Postoperative studies (fig. 5) gave striking results in regard to the sensation remaining. Even more interesting is the fact that the patient referred the touch points to locations quite wide of the points of actual contact as indicated in the diagram. Daily tests were carefully made with her eyes closed, and the findings remained consistent. She was highly cooperative, and I feel that her responses were dependable. The answers were not prompted in any way. A hypothetical explanation of this phenomenon has been given.

The impression was gained at the time of operation that the surgeon operating in 1928 had only partially injured the maxillary peripheral division of the nerve.

17. The operations here reported, representative of both approaches, were well controlled as to observations made at the time of operation, and I feel that there was no trauma to the nerve other than the intended section. The postoperative studies were checked repeatedly by several examiners.

CASE 2.—L. D., a white woman aged 55, was referred to me by Dr. C. B. Busby, of Brooklyn, Iowa, in April 1936.

In March 1935, she had her first "erash" of pain, a terrific paroxysm of short duration over the left maxillary region. The attacks occurred four or five times a day. Touching the lower part of the left side of the nose invariably provoked an attack.

She received an injection of alcohol in July 1935, which lessened somewhat the severity, but not the frequency, of the attacks. The trigger zone on the left side of the nose shifted to the upper gums on the left side, and the attacks began to involve the distribution of the left second and third branches, with an

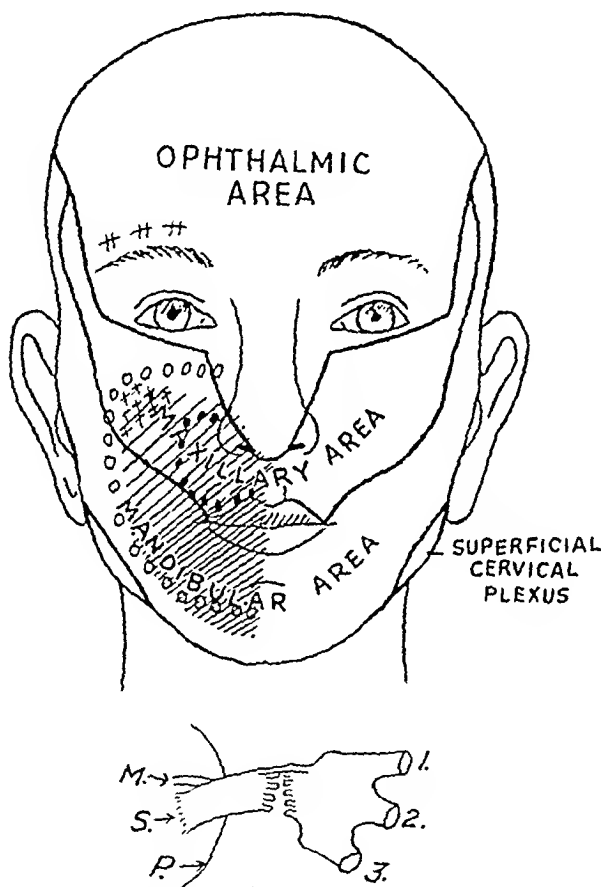


Fig. 5 (case 1).—The single lines mark the area in which the sensation of pain to pinprick was estimated as being about 90 per cent lost. Sensation to touch in this area was about 50 per cent lost. When the patient was touched at the points denoted by the solid black circles she referred the sensation to points denoted by the plain circles. When touched in the region marked by crosses she consistently referred the sensation to the region above the eyebrow marked by double crosses. Herpes developed after the operation on the right side of the lips and chin. The losses of sensation to pain and touch in the buccal mucosa and the right half of the tongue appeared to be about the same as those demonstrated. Corneal sensation and the motor function of the fifth and seventh nerves were intact. No corneal ulcer was present. Subjective numbness was negligible. The drawing at the bottom demonstrates the relative amount of the root sectioned.

occasional involvement of the first division. On rare occasions the right side of the face was involved, but less severely.

On examination there was evidence of a slight loss of sensation to touch and pain over the lower left side of the nose, part of the left cheek and the left side of the upper lip.

After discussing with me the relative merits of total and partial section she chose the partial section, feeling that should the ophthalmic division become too troublesome it could be severed later.

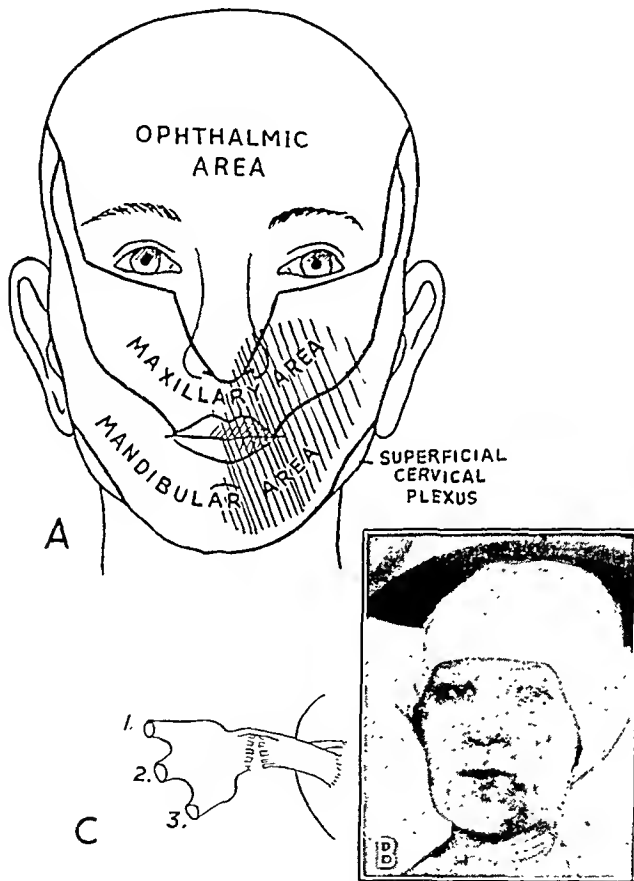


Fig. 6 (case 2).—In the shaded area in *A*, sensation to pinprick was about 90 per cent lost, and to touch was about 50 per cent lost. The cross hatching on the lips represents the area of complete numbness. The buccal mucosa and the left half of tongue presented about the same losses as the regions denoted by the shaded area. *B* shows herpes developed on the lips, the chin and the cheek after the operation, extending about $\frac{1}{2}$ inch across the midline on the chin. Corneal sensation and the function of the motor fifth and seventh nerves were intact. No corneal ulcer was present. Subjective numbness was negligible. *C* demonstrates the relative amount of the root sectioned.

By a left subtemporal exposure the sensory root was exposed, and all its fibers were sectioned except the uppermost fasciculus. The wound healed unevent-

fully. Herpes developed on the left side of the chin, on the left cheek and about the left side of the lips, extending about $\frac{1}{2}$ inch (1.3 cm.) across the midline on the chin.

A sensory loss was found as indicated in figure 6. In this case, which preceded case 1 chronologically, I asked the patient to respond only if she felt the stimulus. I did not ask her to locate it. Hence, information as to referred sensation was not obtained.

The infrequent minor attacks which had involved the ophthalmic division on the left and on the right side were not materially changed after the operation. The major attacks involving the second and third divisions have remained eliminated to the time of writing (one year).

CEREBELLAR APPROACH

CASE 3.—F. B., a white man aged 56, was referred to me by Dr. C. A. Samuelson, of Sheldon, Iowa, in September 1936.

Pain in the right side of the face began in 1911. The attacks lasted for about six months, during which time the patient had some teeth extracted. He was then free of pain until March 1936. He described the pain as an electric shock brought on by cold air, eating or drinking. It was usually confined to the upper lip and the upper part of the cheek on the right side, but occasionally extended to the lower jaw. There was a trigger zone on the lower right side of the nose, the right side of the roof of the mouth and the right side of the upper lip.

The root was exposed through a right cerebellar approach, and slightly more than the lower half was sectioned. The patient's recovery was uneventful except that on the second day after the operation he showed for the first time evidence of slight facial palsy on the right side. This had cleared up, however, at the time of discharge. Studies in sensation revealed the findings shown in figure 7. The sensory losses were so small as to be clinically insignificant.

CASE 4.—F. M., a white man aged 45, was referred to Dr. R. A. Fenton by Dr. L. E. Hooper, of Indianola, Iowa, in August 1936.

In January 1936, pain developed in the right cheek and in both lower jaws. This continued intermittently until June. He had several teeth extracted and was free of pain until August, when pain returned on the right side only. The attacks became more frequent and severe. There was a trigger zone on the right side of the chin, and the pain seemed to involve the second and third branch distribution. He described the pain as giving a feeling "as though a building fell on my face" or "just like a team of horses were pulling my jaw out."

The root of the fifth nerve on the right side was exposed by the cerebellar approach, and half of the root was sectioned. His recovery was uneventful, and sensory studies revealed only moderate diminution in sensation as shown in figure 8. The results were comparable to those in the preceding case. The operative scar and the patient are shown in figure 9. The result from the patient's point of view can be no better expressed than in his own words. When asked if he had noticed that his face felt numb anywhere, he replied in the negative, and then, rubbing his hands over his face, he added, "Doc, if it wasn't for being rid of that awful pain, I wouldn't know I'd been operated on."

CASE 5.—M. D., a white woman aged 72, was referred to me by Dr. B. D. Elliott, of Oskaloosa, Iowa, in January 1937.

Nine years previously she had had a tonsillectomy. An infection of the wound remained for about six weeks. Subsequently, coughing caused a sharp pain in

the right side of the tongue. There was also some loss in control of the tongue, which became somewhat thickened. Touching a spot on the buccal side of the right mandible posteriorly would incite a sharp attack of pain. In 1932 she was given an injection of alcohol, elsewhere, which was repeated in four days. This relieved her attacks for a about a year but induced unpleasant hyperesthesia over the right side of the face. Three more injections of alcohol were given at intervals of three months. The attacks continued to occur more frequently, however, and were severe, appearing to involve the second and third branch distribution on the

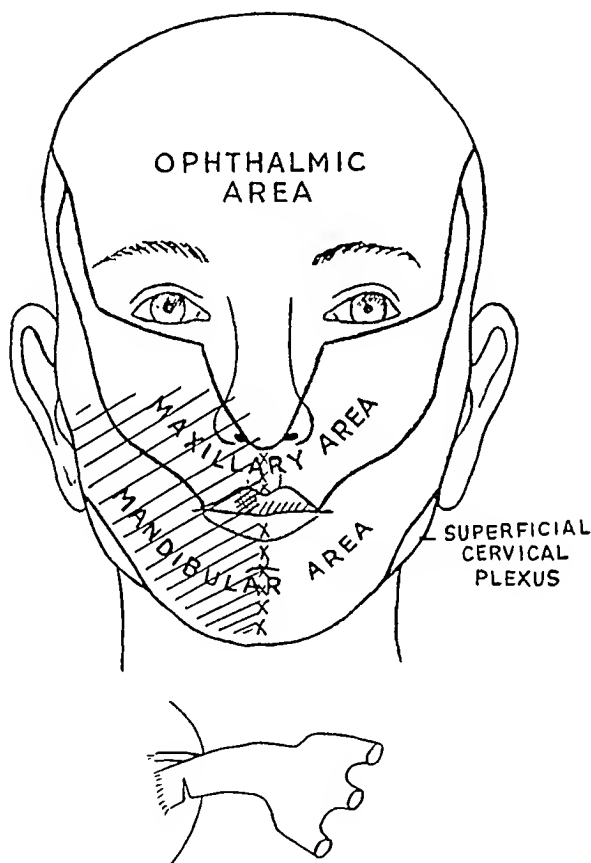


Fig. 7 (case 3).—The shaded area represents the region in which there were about 50 per cent loss of sensation to pinprick and 10 per cent loss of sensation to light touch. Sensation in the tongue and buccal mucosa was about the same. The region denoted by the cross hatching on the lip was completely numb. In the mid-line, represented by crosses, the patient showed hyperesthesia when a pin was dragged from one side to the other. Herpes developed on the right side of the lips after the operation. Corneal sensation and the function of the motor fifth nerve were intact. There was no corneal ulcer present. Subjective numbness was hardly detectable. A slight facial palsy developed on the second day after the operation, from which the patient had almost completely recovered at the time of discharge. The drawing at the bottom demonstrates the relative amount of the root sectioned.

right. She discovered trigger zones on the right side of the tongue, on the right side of the lower lip and on a spot just lateral to the lip. Touching these zones, chewing or eating anything cold invariably incited the attacks, and she presented a typical picture. The face was held rigid, she talked carefully without moving the mouth, she had an anxious expression and she guarded against having her face touched.

Examination revealed a slight dulling of sensation to pinprick in a spotty distribution over the mesial half of the mandibular division.

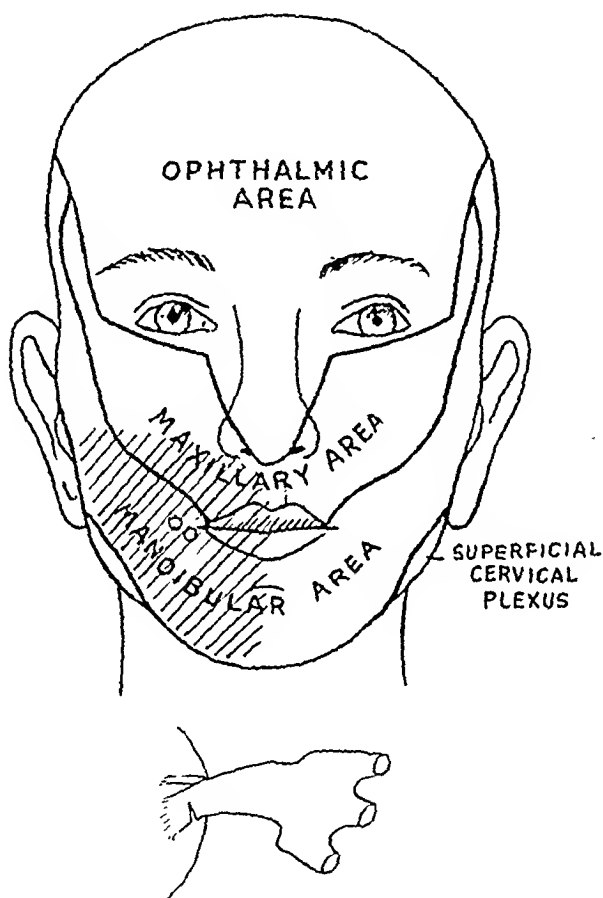


Fig. 8 (case 4).—The shaded area represents the region in which there were about a 25 per cent loss of sensation to pinprick and a hardly detectable loss of sensation to light touch, except in the areas marked by circles, where there seemed to be a complete numbness. Sensation in the tongue and buccal mucosa was about the same as in the region denoted by shadings. Herpes developed on the right side of the lips after the operation. Corneal sensation and the function of the motor fifth and seventh nerves were intact. No corneal ulcer was present. The patient denied feeling numbness to any degree in the face. The drawing at the bottom demonstrates the relative amount of the root sectioned.

The root of the fifth nerve on the right side was exposed by the cerebellar route, and about one third of the root was sectioned with the guillotine knife previously described.



Fig. 9 (case 4).—*A* shows the outline of the mild sensory changes shown in figure 8. *B* shows the scar of the operation. I have subsequently lessened the extent of this incision.

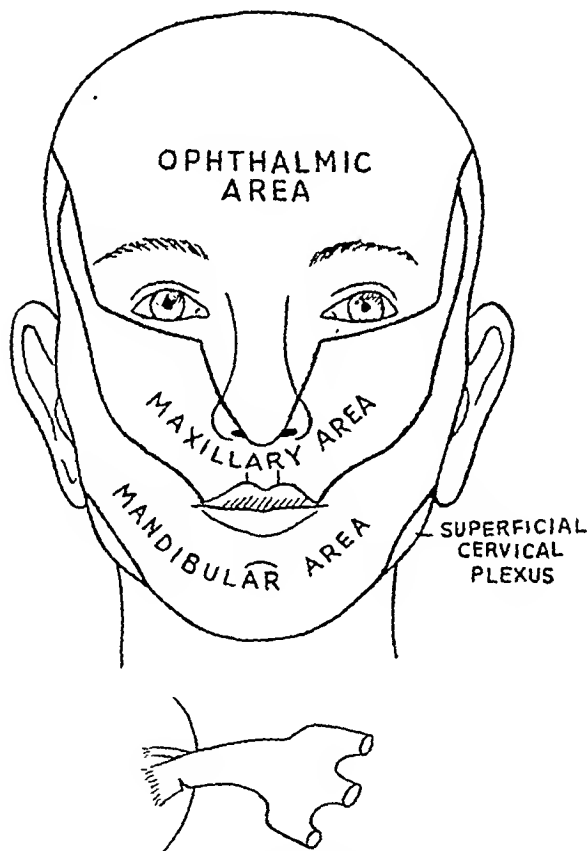


Fig. 10 (case 5).—No additional detectable loss of sensation to pinprick, light touch, pressure, temperature or two point discrimination was present in the face. No loss of sensation to pinprick or to light touch on tongue, lip, gums or buccal mucosa was noted. Herpes developed on the right side of the lips after the operation. Corneal sensation and motor function of the fifth and seventh nerves were intact. No corneal ulcer was present. The drawing at the bottom demonstrates the relative amount of root sectioned.

The patient recovered uneventfully, and repeated sensory examinations revealed no detectable loss in sensation on the tongue, in the buccal mucosa or on the face, except that which had been present before the operation. Heat, cold and pressure were also interpreted normally (fig. 10). The "tic" crises were abolished, and she did not complain of hyperesthesia in the right side of the face. Corneal sensation and the function of the motor fifth and seventh nerves were intact.

Unfortunately, when she was ready for discharge "butterfly" erysipelas developed over the face, with a severe reaction which became complicated by streptococcic meningitis, causing death. Permission for necropsy was denied.

CASE 6.—B. MCC., a white man aged 67, was referred to me by Dr. R. C. Crumpton, of Webster City, Iowa, in May 1937.



Fig. 11 (case 6).—Photograph taken four days after the operation, illustrating a small incision which provides adequate exposure for the operation. The mid-sagittal plane is indicated.

This patient, in addition to having paralysis agitans, had suffered frequent attacks of tic douloureux for five years. The attacks were in the second and third branch distribution on the right. Eating, talking and stroking the upper lip on the right side were inciting stimuli. Several injections of alcohol had been attempted. There had also been an unsuccessful attempt to make an injection into the ganglion. An infection developed in the right temporomandibular joint, with cellulitis of the right side of the face, which was the site of two draining sinuses. The infection precluded further attempt at the injection of alcohol as well as operative attack by the subtemporal route. The attacks were so frequent and so difficult to bear that the patient was eager to have an operative section. Fortunately the tissues posteriorly were not infected, and a partial section of the sensory root was carried out by the cerebellar route. The operation was done

with the area under local anesthesia, and, strangely, as has been pointed out by Dandy, no sensation of pain was induced when the root was sectioned. The inferior two thirds of the root was sectioned with the guillotine knife without the slightest difficulty and with minimal retraction of the cerebellar hemisphere. A greater portion of the root was sectioned than was thought to be necessary, in the hope of diminishing the pain in the jaw from infection. The "tic" was abolished, and after the operation the patient felt no numbness in the face. The department of neurology reported that fully 75 per cent of sensation to touch and pain was preserved in the second and third branch distribution. The pulling of a whisker in this region was keenly felt, though not quite so sharply as in a comparable location on the opposite side.

This case illustrates not only the advantage but the occasional necessity of a cerebellar approach to the fifth cranial root. It is also illustrative of the fact that the section may be accomplished through a relatively small opening (fig. 11).

COMMENT

These representative and carefully studied cases demonstrate, in my opinion, that it probably makes no significant difference from a physiologic standpoint where the root is sectioned, provided comparable sections are made. So far the sections made by the subtemporal route have been far more extensive than those made by the cerebellar route. The subtemporal exposures were the earlier operations. Subsequently I became more courageous in deciding to cut less of the root. Even so, the results with the two exposures indicate a comparability. After developing the cerebellar technic, I have chosen to use it in preference to the subtemporal for technical reasons and I believe that with the guillotine knife the section can be better controlled.

However, there are contraindications for the cerebellar exposure, as Dandy has pointed out, for example, latent mastoid infection on the same side and deafness on the opposite side.

I hope to further these studies by sectioning less of the root by the subtemporal exposure.

In the last analysis, the neurosurgeon should be equipped and skilled to carry out both exposures, and thus lend the flexibility to his decision in the given case that these two excellent operations can provide.

A history of repeated injections of alcohol, particularly in the third branch, may become a contraindication to the subtemporal exposure.

If there exists the slightest doubt concerning the possibility of a tumor in the cerebellopontile angle, the cerebellar approach is the method of choice, and the presence of such a tumor in 5 per cent of Dandy's cases deserves consideration. Obviously a most careful examination of the patient with tic douloureux should be made before the operation with this in mind, and it appears that the presence of any significant organic lesion about the root would be made known by at least a diminishing of the sensitive corneal reflex on the homolateral side. The

patient with "tic" is so wary that the examiner probably often foregoes a careful examination, but for the ultimate good of the patient he should not do so.

INJECTION OF ALCOHOL

There was a time when the injection of alcohol deserved serious consideration as an alternative to section of the root. The most valid argument in its behalf was that it trained the patient to bear the numbness he must permanently endure should he consent to the operation.¹⁸ The situation is now reversed, for the possibilities of partial section of the sensory root offer the patient a cure with no significant subjective sensory loss, while injection of alcohol produces a total sensory loss in branch distribution.

Injection of alcohol should, therefore, take its place among obsolete treatments for tic douloureux. It may occasionally find justified use for patients with operation phobia and for those for whom surgical treatment of any kind would be a decided risk.

Other compromises in the treatment of tic douloureux are seldom deserving of practical consideration at the present time.

SUMMARY

Tic douloureux is discussed from the standpoint of its possible cause and of the paradoxical phenomena that result from partial section of the root. Explanations for the latter are suggested.

It is believed that many of the discrepancies in the results obtained by different operators may be due to degrees of avulsion of the root when the hook or the hook knife is used, of which the operator may not be cognizant. I have designed a guillotine knife which I find useful in obviating this difficulty when making the section at the pons.

The subtemporal and the cerebellar approach are compared on the basis of my experience from surgical and physiologic standpoints. From purely surgical considerations, the cerebellar approach is preferred. From physiologic considerations, it is felt that it makes little difference where comparable sections are made in the root, so far as either the formation of corneal ulcers or the retention of sensation is concerned.

The surgeon should be skilled in making both approaches, and his choice should be determined by careful preoperative examination. The indications and contraindications for the approaches should be evaluated for the given case.

Partial section of the root can be done so as to eliminate the pain crises at least in the second and third branch distribution, and yet with

18. Horrax, G., and Poppen, J. L.: Experiences with Trigeminal Neuralgia and Treatment Employed in Four Hundred and Sixty-Eight Patients During the Past Ten Years, *Surg., Gynec. & Obst.* **61**:394-402 (Sept.) 1935.

losses of sensation in the face so small as to be entirely unnoticed by the patient—a result that leaves little to be desired in the perfection of this operation. The difference between partial and total section of the sensory root is of such great importance to the patient that every effort should be made to spare part of the root. It is my opinion that at least when the surgeon is dealing with pain in second and third branches a total section of the sensory root is an unnecessary mutilation and must be considered an obsolete operation.

CONCLUSIONS

1. A partial section of the sensory root of the fifth nerve can be done so as to abolish the pain crises and with such minimal sensory losses in the face as to cause no inconvenience to the patient.
2. Sensory losses obtained by progressive sectioning of the root are diffusely disposed and seem to be of a combined branch and segmental distribution, with evidence of extensive overlapping.
3. From a surgical standpoint, the cerebellar approach is preferred, but it requires experience in the cerebellar fossa. Greater care is necessary than in the subtemporal approach.
4. From a physiologic standpoint it probably makes no difference, so far as either the formation of corneal ulcers or the retention of sensation is concerned, at what point in the root comparable sections are made.

THROMBOSIS OF THE LEFT INTERNAL CAROTID ARTERY

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Obliteration of one or both carotid arteries has not infrequently been described as part of a widespread obstruction or total occlusion of large arteries given off from the aortic arch. Autochthonous thrombosis limited to the carotid arteries seems to be rare and may in fact never occur without some accompanying change in the cerebral vessels or in the aorta, particularly if considerable time has elapsed since the onset of the primary process. This paper reports 2 instances in which thrombosis was found in the left internal carotid artery and a segment of the thrombosed vessel was excised, in the first case for diagnostic study and in the second case for therapeutic purposes.

When occurring as part of a widespread thrombosis of the large vessels, involvement of the carotid arteries has often been attributed to arteriosclerosis. In some cases no other factors have been mentioned.¹ In many cases other processes, such as syphilis,² traction of

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1. (a) Yelloly, J.: Case of Preternatural Growth in the Lining Membrane Covering the Trunks of the Vessels Proceeding from the Arch of the Aorta, *Med.-Chir. Tr.*, London **12**:565, 1822. (b) Fraenkel, E.: Ueber zwei durch total Verschluss der linken Carotis complicirte Aneurysmen des Aortenbogens [case 2], *Virchows Arch. f. path. Anat.* **79**:509, 1880. (c) Dejerine, J., and Huet, E.: Contribution à l'étude de l'aortite oblitérante, *Rev. de méd.*, Paris **8**:201, 1888. (d) von Weismayr, A. R.: Ein Fall von Stenose der Carotis und Subclavia, *Wien. klin. Wchnschr.* **7**:906 and 925, 1894. (e) Högerstedt, A., and Nemser, M.: Ueber die krankhafte Verengerung und Verschliessung vom Aortenbogen ausgehender grosser Arterien [case 3], *Ztschr. f. klin. Med.* **91**:130, 1897. (f) Erb, W.: Ein Fall von ausgedehnter Gehirnverweichung bei totaler Obliteration der Carotis communis sinistra, München. med. Wchnschr. **51**:946, 1904. (g) Raeder, J. G.: Ein Fall von symmetrischer Karotisaffektion mit praeseniler Katarakt und "Glaukom" sowie Gesichtsatrophie, *Klin. Monatsbl. f. Augenh.* **78**:63, 1927.

(Footnotes continued on next page)

a distorted aortic arch which narrows the mouths of the large arteries at their origin from the aorta,³ embolism⁴ or other inflammatory reactions,⁵ have appeared alone or in association with arteriosclerosis. When the carotid system has been the primary site of the thrombosis in the absence of trauma or tumor, the etiologic factor often has been obscure. More or less circumscribed arteriosclerosis⁶ or nonsyphilitic arteritis⁷ also has been considered, and some reports have offered no suggestion as to the etiologic factor.⁸ Carotid thrombosis associated with hyper-

2. (a) Parsons, C. W.: Case of Occlusion of the Arteries Arising from the Arch of the Aorta, with Aortic Degeneration and Aneurisms, Boston M. & S. J. **9**:400, 1872. (b) Lancereaux, E.: Des affections syphilitiques de l'appareil circulatoire [case, p. 59], Arch. gén. de méd. **2**:42, 1873. (c) Bernard, E.; Gilbert-Dreyfus, and Foulon, P.: Processus d'oblitération complète de l'artère sous-clavière et de la carotide primitive gauches et incomplète de l'artère sous-clavière droite chez un aortique, Bull. et mém. Soc. méd. d. hôp. de Paris **52**:476, 1928. (d) Töppich, G.: Ueber nicht thrombotischen Verschluss der grossen Gefässstien des Aortenbogens, insbesondere des Ostiums der Carotis communis, Frankfurt. Ztschr. f. Path. **25**:236, 1921. (e) Aldrich, A. L.: Occlusion of the Left Common Carotid Artery: Report of a Case, U. S. Nav. M. Bull. **22**:48, 1924.

3. Türk, W.: Arterieller Collateralkreislauf bei Verschluss der grossen Gefässe am Aortenbogen durch deformirende Aortitis, Wien. klin. Wchnschr. **14**:757, 1901.

4. Cohn, cited by Penzoldt.^{6a} Fraenkel,^{1b} case 1.

5. (a) Gull, W. W.: Thickening and Dilatation of the Arch of the Aorta with Occlusion of the Innominata and Left Carotid, and Atrophic Softening of the Brain, Guy's Hosp. Rep. **1**:12, 1855. (b) Savory, W. S.: Case of a Young Woman in Whom the Main Arteries of Both Upper Extremities and of the Left Side of the Neck Were Throughout Completely Obliterated, Med.-Chir. Tr., London **21**:205, 1856.

6. (a) Penzoldt, F.: Ueber Thrombose (autochthone oder embolische) der Carotis, Deutsches Arch. f. klin. Med. **28**:80, 1881. (b) Kussmaul, case 1, cited by Penzoldt.^{6a} (c) Chiari: Ueber das Verhalten des Teilungswinkels der Carotis communis bei der Endarteriitis chronica deformans, Verhandl. d. deutsch. path. Gesellsch. **9**:326, 1906. (d) Harbitz, F.: Bilateral Carotid Arteritis [case 4], Arch. Path. **1**:499 (April) 1926. (e) Houwer, A. W. M.: Thrombose der Arteria carotis mit orbitalen Komplikationen, Arch. f. Augenh. **99**:240, 1928. (f) Wüllenweber, G.: Fortdauer des Lebens bei doppelseitigem vollständigem Verschluss der Aa. carotides internae, Deutsche Ztschr. f. Nervenhe. **105**:283, 1928.

7. Harbitz,^{6d} case 1.

8. (a) Elschnig, A.: Ueber den Einfluss des Verschlusses der Arteria ophthalmica und der Carotis auf das Sehorgan, Arch. f. Ophth. **39**:151, 1893. (b) Agatston, S. A.: Thrombosis of the Carotid and Middle Cerebral Arteries with Bilateral Hemorrhagic Optic Neuritis, Arch. Neurol. & Psychiat. **24**:1245 (Dec.) 1930. (c) Hyland, H. H.: Thrombosis of Intracranial Arteries [case 3], ibid. **30**:342 (Aug.) 1933.

tension has occasionally developed in the presence of abnormal reactions of the carotid sinuses, but the mechanism of this process has not yet been thoroughly worked out.⁹

REPORT OF CASES

CASE 1.—A Russian aged 47 years was admitted to the Peiping Union Medical College Hospital on Dec. 27, 1935. Although he had suffered considerable hardship and poverty during his life, he repeatedly denied trauma or infections other than "colds," "stomach trouble" at the time of the World War and gonorrhea twenty years previously. He denied having had syphilis. Since about 1930 there had been increasing difficulty with vision. In the early spring of 1935, while working in timber concessions in Manchuria, he began to have short periods of numbness in the right arm and leg, for which he was admitted to the hospital of the Chinese Eastern Railway. On discharge he found work as a switch operator on the Chinese Eastern Railway at Harbin at the time the Japanese took over the administration of the railway. A friend stated that even then the patient was nervous, talkative, absent-minded and forgetful, concentrated on himself and worried about his physical condition. In the summer of 1935 he complained of being tired by the long hours of work and headaches, and his poor eyesight prevented him from seeing the railroad signals clearly from a distance. About a month after starting his work he threw a switch the wrong way and caused the wreck of a locomotive and seven empty freight cars. On one occasion he fell down while at work, with temporary "paralysis" of the right side and inability to talk. He was readmitted to the hospital of the Chinese Eastern Railway for a short time, after which he returned to the same work. By September 1935 he was "nervous all the time" and was subject to almost constant headache and to occasional attacks of weakness of the right side. His correspondence with his friends became disorganized, and on their advice he finally left Harbin, coming to Peiping on Dec. 9, 1935. At that time he seemed constantly worried, had much difficulty in expressing himself, was slow to understand what was said to him and appeared emotional, with rather frequent exhibitions of tears.

On admission to the Peiping Union Medical College Hospital his complaints were of headache, cold sensations in the right arm, the feeling that the right arm had dropped off, attacks of weakness in the right arm and leg, with accompanying inability to speak, impairment of memory, inability to find the words he wanted, noises in the head, poor vision, difficulty in sleeping and general nervousness.

Physical examination showed vision of 6/9 in each eye and concentric constriction of the visual fields but no consistent disturbance of motility, of sensation to objective tests or of the reflexes. There was gross difficulty in word finding, the patient being unable to express himself consecutively for more than a sentence or two and often being unable to produce a single word promptly in answer to a simple question about himself. Naming objects and colors, calculation, memory for sequence of remote and recent events, and right-left orientation of the body were all

9. (a) Hiller, F.: Die Zirkulationsstörungen des Rückenmarks und Gehirns, in Bumke, O., and Foerster, O.: *Handbuch der Neurologie*, Berlin, Julius Springer, 1936, vol. 2, p. 409. (b) Marinesco, G., and Kreindler, A.: *Oblitération progressive et complète des deux carotides primitives; Accès épileptiques, considérations sur le rôle des sinus carotidiens dans la pathogénie de l'accès épileptique*, Presse méd. 44:833, 1936.

markedly impaired. The results of additional psychologic tests are given in table 1. The Wassermann reaction of the blood was negative; the blood pressure was 100 systolic and 62 diastolic. On Feb. 12, 1936, one of us (H. H. L.) exposed the left carotid arteries, with the intention of injecting colloidal thorium dioxide for arterial encephalography. A needle was inserted into the internal carotid artery just distal to its point of origin. As the needle passed into the vessel the resistance of a solid structure was encountered, and it was impossible to withdraw blood. Repeated punctures were made in various directions with the same result. The

TABLE 1.—*Psychologic Tests Before and After Operation (Case 1)*

Tests	Before Operation		After Operation	
	Results	Date	Results	Date
Retention of digits (forward)....	4 digits; mental age, 4 yr.	Jan. 15	5 digits; mental age, 7 yr.	Feb. 20
Retention of digits (backward).. Naming of colors.....	Failed None	Jan. 15 Jan. 15	Failed Named correctly 3 in 5	Feb. 20 Feb. 20
Immediate visual memory..... Diagonal form board.....	Poor Time, 3' 18"; errors, 37	Jan. 17 Jan. 17	Improved (?) Time, 1' 42"; errors, 27	Feb. 20 Feb. 20
Five figure form board.....	Errors, 26; time, 3' 30"	Jan. 20	Errors, 30; time, 2' 39"	Feb. 20
Casuist form board.....	Errors, 17; time, 4' 20"	Jan. 20	Errors, 15; time, 1' 54"	Feb. 20
Two figure form board..... Cube knob.....	Failed Mental age, 6 yr.	Jan. 18 Jan. 15	Failed Mental age, 6 yr.	Feb. 20 Feb. 25
Repeating of syllables..... Mental arithmetic test.....	Mental age, 3 yr. Mental age, 6.3 yr.	Jan. 15 Jan. 23	Mental age, 5 yr. Mental age, 5.3 yr.	Feb. 25 Feb. 21
Graded direction test..... Maze test.....	12% (mark) Mental age, 13 yr. 6 mo.	Jan. 22 Jan. 13	20% Mental age, 12 yr.	Feb. 21 Feb. 27
Direction test..... Immediate logical memory.....	Mental age, 5.7 yr. Remembered 1/18 of material	Jan. 22 Jan. 18	Mental age, 6.2 yr. Remembered 7/18 of material	Feb. 25 Feb. 27
Drawing of human being.....	With double profile	Jan. 23	Much better; without double profile	Feb. 22
Clock tests				
Direct imitation..... Clock set to oral commands.... Telling the time.....	50% 0% 20%	Jan. 21 Jan. 21 Jan. 21	55% 0% 30%	Feb. 26 Feb. 26 Feb. 26
Written commands Reading commands..... Setting clock.....	80% 0%	Jan. 24 Jan. 24	100% 20%	Feb. 27 Feb. 27
Coin bowl test				
Oral commands..... Written commands in full (not read aloud)..... Written commands in full (read aloud) Reading commands..... Following out commands.... Written commands in abbreviation.....	17% 23% 75% 58% 83%	Jan. 23 Jan. 23 Jan. 23 Jan. 23 Jan. 23	92% 50% 42% 42% 67%	Feb. 26 Feb. 26 Feb. 26 Feb. 26 Feb. 25

needle was then inserted into the lumen of the common carotid artery proximal to the point of bifurcation, and with the external carotid artery occluded by digital pressure, 10 cc. of thorium dioxide was injected. A roentgenogram which was taken as the injection was completed showed that none of the contrast medium had entered the internal carotid artery. Accordingly a small segment of the latter vessel was excised between ligatures of doubled medium-sized silk. The lumen of the artery was found to be filled completely with grayish material which on microscopic examination proved to be an organized thrombus.

On February 22 the patient said he felt much better and could "speak without stuttering." There was less numbness in the right arm, less noise was heard in

the head and sleeping was improved. He said, "Everything is much better." On February 23, 24 and 26 there was some headache, and the patient said he felt "nervous," but on February 27 he was free from headache, and on the following day he announced that he felt "physically well." Psychologic tests were repeated, and they confirmed a definite improvement in mental functions, as shown in table 1. The patient grew restless in the hospital and insisted on leaving, so he was discharged on March 2. He soon afterward went back to Harbin, and further word from him has not been obtainable.

CASE 2.—A Chinese student of mathematics aged 27 years was admitted to the Peiping Union Medical College Hospital on April 2, 1937. Thirteen months previously, while talking to friends at school, he suddenly became unable to speak. He started at once to walk home and fell down on the way without losing consciousness. He was taken by rickshaw to his residence in the city and the next day proceeded by rickshaw to his family's home in the country. He felt drowsy

TABLE 2.—*Blood Pressure Before and After Operation (Case 2)*

Blood Pressure,		Blood Pressure,		Blood Pressure,	
Date	Mm. Hg, Left Arm	Date	Mm. Hg, Left Arm	Date	Mm. Hg, Left Arm
April 2.....	184/140 (200/142 right arm)	May 10.....	172/134 148/128	May 27.....	138/ 90 124/ 90
4.....	142/104	11.....	184/138	28.....	130/100
5.....	182/142		172/130	29.....	126/ 90
7.....	152/111	12.....	178/138	June 2.....	128/ 90
11.....	154/118	13.....	188/138	3.....	132/ 96
12.....	152/104	14.....	170/138		124/ 90
17.....	164/122	15.....	168/128	4.....	120/ 88
21.....	146/110	16.....	160/120	5.....	124/ 88
24.....	148/ 98	17.....	160/120	6.....	126/ 88
25.....	146/ 96	18.....	152/110	7.....	124/ 88
26.....	156/104	19.....	150/100	8.....	134/ 84
May 1.....	150/100	20.....	150/110	9.....	120/ 74
2.....	140/100	21.....	152/102	11.....	130/ 90
3.....	154/100	22.....	130/ 90	14.....	130/ 92
7*.....	162/114	23.....	130/ 90	18.....	124/ 82
8.....	150/118	24.....	136/ 90	19.....	122/ 80
	170/130	25.....	140/100	20.....	118/ 80
9.....	178/142 190/136	26.....	138/ 94		

* Operation.

and somewhat "confused," but he knew where he was and with whom he was. Beginning on the second day paralysis and numbness of the right side gradually developed. He was unable to read Chinese characters, and for three months could make sounds but could not enunciate clearly. He then began to learn little by little to say some things intelligibly. Soon afterward he started to walk. He had to be fed for six months. With considerable effort he learned to read some characters and taught himself to write them with his left hand, but for six months his condition had been physically and mentally almost stationary.

On admission to the hospital he was found to have hypertension (table 2) without cardiac enlargement. The neurologic examination showed his vision to be: left, 6/30; right, 6/20. There were nasal hemianopia of the left eye and contraction of a sector of the upper temporal field of the right eye, retinitis pigmentosa and hypertension of the retinal vessels. There was hemiplegia of the right side (the arm chiefly) of distal type, with corresponding signs of involvement of the pyramidal tracts and reduction of sensation of all sorts, including discrimination of form, weight, texture and Chinese characters traced on the skin, on the right side. There also was pronounced motor and receptive aphasia, calculation, reading and writing being especially affected. Details of

the psychologic tests before and after operation are given in table 3. Palpation of the common carotid arteries showed less amplitude of pulsation on the left side. Pressure over the right carotid sinus gave no indication of hypersensitivity of that structure. Pressure over the left sinus was consistently followed by deep and irregular respiration and by dizziness, but there was no change in pulse rate or blood pressure. Digitalization increased the effect of pressure over the left carotid sinus. The Wassermann reaction was negative for both blood and cerebrospinal fluid. On May 7 one of us (S. T. K.) exposed the carotid arteries on the left side and denervated the left carotid sinus. Thorium dioxide was then

TABLE 3.—*Psychologic Tests Before and After Operation (Case 2)*

1. Motor Tests Before and After Operation		
Motor tests	Before Operation	After Operation
Speed of cutting S.....	24 min. 10 sec.	13 min. 10 sec.
Errors of cutting S.....	118.8 mg.	51.2 mg.
Speed of cutting star.....	38 min. 17 sec.	28 min. 32 sec.
Errors of cutting star.....	262.4 mg.	158.6 mg.
Tapping	174 in 30 sec.	178 in 30 sec.
Strength of right hand.....	1 Kg.	4 Kg.
Strength of left hand.....	32 Kg.	41.8 Kg.
Handwriting	Steadier and better in strokes and fewer reversed words
Speed of handwriting.....	3½ words in 40 sec.	13 words in 40 sec.
Tactile recognition of objects		
Right hand.....	Number of correct answers, 17%; average speed, 8 sec.	Number of correct answers, 8%; average speed, 6.3 sec.
Left hand	Number of correct answers, 79%; average speed, 10.3 sec.	Number of correct answers, 71%; average speed, 9.1 sec.
2. Mental Tests Before and After Operation		
Mental tests		
Intelligence tests	I. Q., 48	I. Q., 54
Interpretation of pictures.....	44%	33%
Solution of problem situations.....	75%	60%
Form analysis	67%	84%
Repetition of digits.....	30%	30%
Repeating digits backward.....	14%	14%
Immediate reproduction of cube tapping..	33%	66%
Immediate reproduction of a paragraph..	27%	46%
Reorganization of dissected sentences.....	0%	0%
Clock tests	Errors, 8; aver- age speed, 71 sec.	Errors, 8; aver- age speed, 54.7 sec.
Immediate visual memory.....	50% correct	50% correct
Understanding of separate abstract words....	57% correct	50% correct
Reading of different words.....	56%	76%
Understanding of the reading.....	15.8%	18%
Drawing	More details but same as before in general
Chinese puzzles	13%	66%

injected into the left common carotid artery, and a roentgenogram was taken near the end of the injection. It showed filling of the external carotid artery and its branches but complete lack of visualization of the internal carotid artery. A small needle was then introduced into this vessel. It met uniform resistance, and blood could not be withdrawn, although the needle was finally pushed deliberately all the way through the artery. Complete occlusion being demonstrated, a segment of the artery was excised, and the lumen was shown to be completely filled with an organized thrombus, as in case 1. After operation there was not much change in the condition of the patient. The blood pressure rose and then fell below the initial pressure, as shown in table 2. Resistance of the right arm

to passive movement on daily manipulation became somewhat less, and the patient became able to move the fingers of his right hand in isolated flexion and extension without overflow of movement to the whole arm, a procedure which he had not been able to carry out before the operation. He showed some subjective improvement in speech, but the psychologic tests demonstrated only slight improvement, if any, in mental function (table 3).

COMMENT

The symptoms of occlusion of the carotid artery have been discussed in an extensive literature on ligature of the carotid artery and will not be reviewed here. Information gained by the mental tests in the 2 cases reported in this paper, however, deserves comment. The results of a number of tests of general intelligence showed a rather uniform reduction of performance. This does not necessarily prove diffuse damage to the brain. The majority of tests commonly used to measure general intelligence are based on the use of words, often with special reference to word finding, the use of figures and the appreciation of certain visual relations. These functions have some local representation in the left parieto-occipital region of the brain in right-handed persons. With some appreciation of this emphasis in the structure of tests of intelligence, Kleist¹⁰ stated that intellectual disturbances increase in frequency and severity the closer the site of the wound is to the occipital lobes and to the region of sensory speech. Mental tests have considerable value, but their interpretation must be made from a broad point of view. Case 1 illustrates the difficulty in interpretation. The only consistent symptoms were concentric constriction of the visual fields and a reduction of mental performance, which included defective word finding, calculation, right-left orientation of the body and memory. This suggested to one of us (R. S. L.) the original diagnosis of a vascular lesion in the left parieto-occipital region. It was the expectation of demonstrating such a condition that led to arterial encephalography, which provided the unexpected demonstration of thrombosis of the left internal carotid artery. But even here, one is not justified in discarding all localizing value of these mental tests in view of the frequent occurrence of embolus or thrombosis or other vascular pathologic conditions in the brains of patients with carotid thrombosis examined at autopsy.¹¹ Terminal branches of the middle cerebral artery appear to be most affected after occlusion of the carotid artery, and so the mental functions having some representation in the left parieto-occipital distribution

10. Kleist, K.: *Gehirn Pathologie vornehmlich auf Grund der Kriegserfahrungen*, Leipzig, Johann Ambrosius Barth, 1934, p. 550.

11. Fraenkel.^{1a} Erb.^{1f} Lancereaux.^{2b} Gull.^{5a} Penzoldt.^{6a} Chiari.^{6c} Harbitz.^{6d} Houwer.^{6e} Wüllenweber.^{6f} Elschmig.^{8a} Agatston.^{8b} Hyland.^{8c} Hiller.^{9a} Marinnesco and Kreindler.^{9b}

of these terminal arteries might be expected to be affected. A still wider point of view would take into account the importance of the left parieto-occipital region during evolution. The parietal lobes have undergone the greatest increase in volume, more than that of the much vaunted frontal lobes.¹² The ability to construct and use to an increasing degree of complexity such symbols as words, graphic signs and figures in calculation has a definite relation to the left parieto-occipital area. Since this aspect of intelligence is a high point in evolution, it might be one of the functions to be first and most markedly affected by any generalized disturbance such as toxemia or interference with the nutrition of the whole brain.

To summarize, in the 2 cases reported in this paper, mental tests showed a reduction of general intelligence, but this must be interpreted with caution since it may represent a diffuse change in the brain, perhaps nutritional, or it may indicate focal secondary damage in the most salient part of the vascular tree which springs from the left internal carotid artery. The frequency of secondary vascular lesions in the parietal lobes in cases of carotid occlusion makes the latter possibility seem likely. For the practical purposes of this paper the mental tests are not included with reference to localization in the brain but serve merely to indicate the comparison of the conditions before and after operation. From this standpoint the results seem important enough to be recorded in some detail in tables 1 and 3.

The response to pressure on the carotid sinuses unfortunately was not noted in case 1. In case 2, pressure on the right carotid sinus had no effect, while pressure on the left sinus uniformly caused deep and somewhat irregular breathing and dizziness but did not produce any significant change in pulse rate or blood pressure. These symptoms were intensified by digitalization. This was regarded as a somewhat abnormally sensitive sinus reaction of "cerebral type"¹³ and, in conjunction with a palpably reduced amplitude of pulsation in the left common carotid artery and fluctuation of the blood pressure between 142 systolic and 104 diastolic and 200 systolic and 142 diastolic, led to the recommendation of surgical exploration of the left carotid region. It was predicted that denervation of the left carotid sinus would be followed by a rise of blood pressure which would later fall to a level

12. Weidenreich, F.: Observations on the Form and Proportions of the Endocranial Casts of *Sinanthropus Pekinensis*, Other Hominids and the Great Apes: A Comparative Study of Brain Size, *Palaeontologia Sinica*, s. D. (no. 4), 1926, vol. 7.

13. Weiss, S.; Capps, R. B.; Ferris, E. B., and Munro, D.: Syncope and Convulsions Due to a Hyperactive Carotid Sinus Reflex, *Arch. Int. Med.* 58:407 (Sept.) 1936.

controlled by the presumably normal right sinus together with the other cardiovascular regulatory mechanisms. After denervation of the sinus and excision of a segment of the thrombosed carotid artery, the blood pressure behaved as expected (table 2). The exact role of the sinus in this case cannot be known, but it seems clear that it played an important part in the hypertension. An attractive hypothesis would be that the abnormal sinus reaction on the left side exposed the brain to bouts of high pressure under circumstances in which the blood was forced in freely through the vertebral arteries and the right carotid artery but not through the left carotid artery; this unbalanced increase of pressure seemed to intensify the difficulty of maintaining adequate blood flow through the smaller branches of the left middle cerebral artery and so hastened or actually brought about destruction of ganglion cells in this area of anoxemia. A direct reflex action on the cerebral vessels by the carotid sinus has been proposed¹⁴ and, if existent, would have a good setting for exhibiting its influence in this case. Another type of effect of the carotid arteries on cerebral circulation may be due to sympathetic fibers carried up the carotid arteries to the cerebral vessels. In the words of Leriche,¹⁵ an "obliterated artery ceases to be an artery and becomes a diseased sympathetic nerve."

The etiologic factor in carotid thrombosis is not known. In neither case reported here was there positive evidence of syphilis. In case 1 there was some bulging of the aorta to the right, with a markedly wide arch on fluoroscopy, but no other sign of arteriosclerosis or of hypertension was presented. In case 2 there was definite and variable hypertension, but its etiologic relation to the carotid sinuses, on the one hand, and to the carotid thrombosis, on the other, is in no way clear to us. It may be significant that in both cases there was an increase of fibrous tissue around the carotid arteries. In case 1 the tissues in the neighborhood were more difficult to separate than usual, normal cleavage planes being partly obliterated as though an old inflammatory process had been present. However, a definite source of a local inflammatory process in the neck could not be found on physical examination or on repeated questioning of the patient. In case 2 there was an unusual amount of fibrous tissue outside as well as inside the carotid sheath. The reports of the pathologic examination of the excised arterial seg-

14. Ask-Upmark, E.: The Carotid Sinus and the Cerebral Circulation, Copenhagen, Levin & Munksgaard, 1935, pp. 23-37 and 262-266. Gollwitzer-Meier, K., and Schulte, H.: Das Verhalten der Hirndurchblutung bei Reizung der Sinusnerven, *Arch. f. exper. Path. u. Pharmacol.* **165**:685, 1932. Bouckaert, J. J., and Jourdan, F.: Sinus carotidiens et circulation cérébrale, *Compt. rend. Soc. de biol.* **121**:1354, 1936.

15. Leriche, R.: Arterectomy in the Treatment of Localized Arterial Obliterations, *Am. J. Surg.* **14**:55, 1931.

ments offer no explanation of the cause for the thrombosis, but there is comment on the absence of any significant arteriosclerotic change in the walls of the arteries.

In case 1 no treatment was intended; excision of a segment of the artery was carried out for diagnostic purposes. It happened that the patient felt better after the operation; mental tests originally given for a different purpose were repeated, and they confirmed the improvement in mental performance. In case 2 the treatment was deliberately two-fold: denervation of an abnormally reacting carotid sinus and excision of a thrombosed carotid artery.

The literature on denervation of the carotid sinus gives few clinical data relating to prophylaxis against pathologic conditions of the cerebral blood vessels. The procedure sometimes has been aimed at the production in persons with low pressure of a higher pressure, which in fact would be only temporary.¹⁶ It seems to us that its main value might lie in the prevention of cerebral ischemia by relieving irregular hypertension due to a hypersensitive sinus. Theoretically this is possible, and the course of the blood pressure in case 2, so far as it goes, suggests that the denervation of the sinus made the brain safer from the effects of the previously existent irregularly high blood pressure and perhaps also from reflex effects on the cerebral vessels from the region of the carotid sinus and carotid artery.

Excision of a segment of the thrombosed carotid artery was carried out in accordance with the principles described by Leriche.¹⁵ This procedure could influence the cerebral circulation, especially in the distribution of the left middle cerebral artery, and thereby improve the corresponding mental functions. It was not technically easy to remove the entire obliterated internal carotid artery, and for this reason it was not done, in spite of Leriche's recommendation that the entire occluded artery be resected. But at least the removal of a thrombosed segment interrupted the continuity of sympathetic impulses in the walls of the artery. Definite improvement followed this procedure in case 1. This cannot be attributed to psychologic influence alone. The pathologic observations were explained to the patient soon after the operation. He did not expect a cure from the operation, and he was also growing restless in the hospital even before the postoperative testing was completed. The improvement must be regarded as an increase in actual mental ability to perform the tasks and was obviously not due to a better attitude or more concentrated effort in doing the tests. The factor of learning cannot play a significant part in view of the large battery used in the testing and the fact that each task was done only twice.

16. Leriche, R.; Fontaine, R., and Froehlich, F.: L'énervation sinu-carotidienne est-elle permise au point de vue physiologique? *Presse méd.* 43:1217, 1935.

once before and once after the operation. It should be noted that in case 1 relatively little neurologic evidence of irreversible damage to the brain was presented even before the operation. In case 2 the results of operative therapy were not so striking. There were a little increase in facility of individual movements with the right hand and fingers, some change in subjective sensation on the right (feeling of warmth, etc.), subjective improvement in word finding and writing, and better speed and accuracy in tests of motility, including handwriting; but from other mental tests there was only slight objective evidence of any significant improvement in mental ability. In contrast to case 1, in case 2 there was a history of a stationary condition for several months before the operation, during which the motor, sensory and mental findings implied considerable irreversible damage to the brain.

Finally, the experience gained in these 2 cases suggests a therapeutic formula. For a patient with symptoms of a cerebral vascular disturbance in the parietal region, with a unilateral reduction of pulsation in the common carotid artery and with a unilateral abnormal response of the carotid sinus on the same side, especially in the presence of hypertension, surgical exploration of the extracranial carotid system seems justified. In such cases denervation of the sinus may have prophylactic value against further damage to the cerebral blood vessels. Moreover, at the time of the exploration the carotid arteries can be examined, and if thrombosis is found, excision of the thrombosed artery may be carried out. The degree to which this procedure may be therapeutically effective will be limited by the extent of irreversible damage to the brain cells which has already taken place before the operation.

SUMMARY

Two cases of thrombosis of the left internal carotid artery of undetermined etiologic origin are reported. The first patient had relatively little evidence of irreversible damage to the brain and after a segment of the thrombosed artery was excised showed definite improvement in subjective feelings and in the performance of mental tests. The second had hypertension and signs of considerable damage to the brain. After denervation of the left carotid sinus and excision of a segment of the thrombosed artery, the blood pressure rose and then fell to a rather constant normal level. There were definite improvement in subjective feelings and in some motor abilities but only slightly better performance of other mental tests.

The syndrome consisting of signs of vascular disturbance in the distribution of the middle cerebral artery, with unilateral reduction in amplitude of pulsation in the common carotid artery and unilateral abnormal reactions of the carotid sinus on the same side, especially if

hypertension is present, is proposed as adequate indication for surgical exploration of the extracranial carotid system. In such cases denervation of the carotid sinus may have prophylactic value against later ischemic changes in the brain by protecting it from excessive alterations of blood pressure due to the hypersensitive sinus and perhaps by interrupting an abnormal chain of reflexes between the carotid artery and the cerebral vascular system. At operation, if thrombosis of the carotid artery is found, excision of a thrombosed segment may be definitely therapeutic but may be limited by the degree of the previous damage to the brain.

PILONIDAL SINUS

SCLEROSING METHOD OF TREATMENT

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AND

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The pilonidal sinus is an extremely interesting and troublesome lesion and has been the subject of much speculation and study. It is more common than physicians are wont to believe and is often unrecognized or confused with other lesions. It is found posterior to the sacrum and the sacrococcygeal region and is variously described as sacrococcygeal cyst, dermoid, coccygeal fistula, a sacral sinus or postanal dermoid. This confusion is characteristic not only of the nomenclature but also of the etiology, pathology and treatment.

The purpose of this paper is twofold: first, to review briefly the subject of pilonidal sinus, because this information may be essential in determining the operative method to be employed; second, to report and discuss four years of experience with the use of a sclerosing solution in the treatment of this disease.

ETIOLOGY

There are two prevalent theories of the cause of pilonidal sinus. The first, advanced by Tourneux and Herrmann¹ in 1887, is that the condition is due to the persistence of coccygeal vestiges of the neural canal. Mallory² in 1892, Oehlecker³ in 1926, Gage⁴ in 1935 and others made worthy contributions advocating this embryologic theory of the formation of the pilonidal sinus. The second theory, postulated by Lannelongue⁵ from 1882 to 1886, is in effect that these sinuses are due to faulty median skin agglutination of the sacrococcygeal region. Lannelongue was supported in this contention by Aschoff⁶ in 1895, Stone⁷

From the proctologic service of the Elgin State Hospital.

1. Tourneux, F., and Herrmann, G.: *J. de l'anat. et physiol.* **23**:498, 1887.
2. Mallory, F. B.: *Am. J. M. Sc.* **103**:263, 1892.
3. Oehlecker, F.: *Deutsche Ztschr. f. Chir.* **197**:262, 1926.
4. Gage, M.: *Pilonidal Sinus: Explanation of Its Embryologic Development*, *Arch. Surg.* **31**:175 (Aug.) 1935.
5. Lannelongue: *Bull. méd., Paris* **3**:371, 1889; *Bull et mém. Soc. de chir. de Paris* **7**:185, 1882; **12**:460, 1886.
6. Aschoff, L.: *Cysten*, in Lubarsch, O., and Ostertag, R.: *Ergebnisse der allgemeinen Pathologie*, Wiesbaden, J. F. Bergmann, 1895, p. 456.
7. Stone, H. B.: *Ann. Surg.* **79**:410, 1924; **94**:317, 1931.

in 1924, Breidenbach and Wilson⁸ and also by Fox⁹ in 1935, and many others. It is imperative, therefore, to bear in mind that, assuming that the earlier theory of Tournoux and Herrmann is correct, a communication may exist directly between a pilonidal sinus and the neural canal, or it may exist indirectly through an anterior tumor. In such an instance the method of treatment here to be advocated is definitely contradicted.

PATHOLOGIC PICTURE

The pathologic condition consists of an acute or chronic inflammation of a localized area in the sacrococcygeal region. A single, skin-lined round or oval orifice is seen in the midline about $1\frac{1}{2}$ to 2 inches (3.7 to 5 cm.) from the tip of the coccyx. This orifice, from which a tuft of fine silky hair may protrude (this was seen in only 2 cases in our series), leads into a skin-lined main tract (fig. 1 *A*). The tract varies in length from 3 to 7 cm. It runs upward and occasionally downward for a very short distance unless it is associated with a fistula in ano like that in the case reported by Warman.¹⁰ One of our patients presented this rarity. A bulbous pouch (fig. 1 *B*) is frequently found at either end of the tract; or there may be a number of sacculations, existing as separate cavities, which may communicate with each other or with the main tract by means of lateral tracts; or some of these may drain through external orifices in the skin. Subsidiary orifices caused by extension of the infective process may be found in the midline or to one or the other side of it. These vary in size, are irregular and discolored and are usually filled with granulation tissue and purulent material.

The dispute as to the histologic picture is interesting. Breidenbach and Wilson⁸ maintained that the cutaneous appendages described by others could not be found. They detected areas of acute or chronic inflammation with numerous foreign body giant cells, some hair without the hair follicles, small islands of squamous cells, either free or doubtfully attached to the lining of the cyst, and squamous epithelium at the entrance of the sinuses. Oehlecker³ made careful microscopic studies, including serial sections, but found no epithelial structures. Neither was nerve tissue seen by these observers, although Gage,⁴ in his study of the subject, described glial tissue beneath the epithelial lining in lesions which extended as far as the dura. However, the presence of cutaneous appendages, such as hair follicles, sebaceous glands and sweat glands, described by Gussenbauer¹¹ in 1892 and by Crone¹² in 1917 as

8. Breidenbach, L., and Wilson, H. L.: *Ann. Surg.* **102**:455, 1935.

9. Fox, S. L.: *Surg., Gynec. & Obst.* **60**:137, 1935.

10. Warman, W. M.: *West Virginia M. J.* **32**:80, 1936.

11. Gussenbauer, C.: *Prag. med. Wchnschr.* **18**:441, 1893.

12. Crone, E.: *München. med. Wchnschr.* **64**:521, 1917.

appearing in the cystic tissue of such lesions, was confirmed recently by Stone,⁷ Fox,⁹ Rogers and Hall¹³ and others.

Since no radical excisions were performed in the cases in our series, we secured only small sections of tissue for study. Figure 2 shows a section taken from a typical sinus ending in a pouch. A well developed hair follicle surrounded by connective tissue, round cell infiltration and fat cells, was the only one discovered deep under the epithelial surface.



Fig. 1.—*A*, typical appearance of a chronic pilonidal sinus. The sinus is situated, as usual, in the midline of the sacrococcygeal region. Mercurochrome has been applied for visualization of the multiple orifices. The distal orifice is skin lined and is the congenital opening into the sinus. The one immediately above and another at the proximal end and to the left are secondary to a spontaneous rupture of abscesses, the latter being considerably larger, gaping, elevated and inflamed. Two pouches were found communicating with the main tract, the lower one draining through the small openings and the upper one draining indirectly through the large ragged opening. This proximal pouch was completely filled with fine hair packed tightly into a ball. *B*, roentgenogram of a pilonidal sinus after the injection of iodized poppyseed oil. The narrow tract terminates in a pouch at the proximal end.

13. Rogers, H., and Hall, M. G.: Pilonidal Sinus: Surgical Treatment and Pathologic Structure, *Arch. Surg.* **31**:742 (Nov.) 1935.

The sinus from which this section of tissue was taken was injected with iodized poppyseed oil and a roentgenogram was taken (fig. 1 *B*), as suggested by Brams.¹⁴

DIAGNOSIS

Despite the fact that the lesion characteristic of this disease is typical, the condition is frequently misdiagnosed. A thorough proctologic examination, including sigmoidoscopic, anoscopic and roentgenologic study, should be made in every case before any treatment is decided on or attempted. In the early stage, when no infection is present, one may find only a dimpling of the skin or a small skin-lined orifice leading into a tract directed upward for a variable distance. When the condition is acute, there are tenderness, swelling and redness over the lower part of

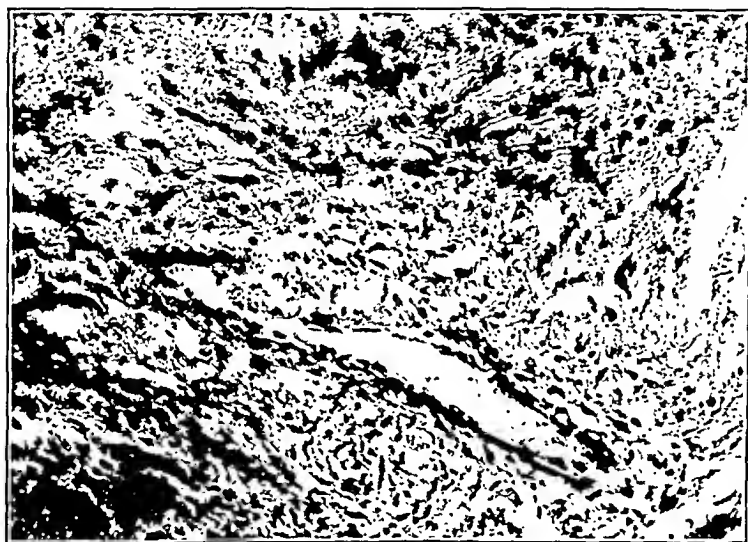


Fig. 2.—Section of tissue removed from the cystic portion of a sinus, showing a well developed hair follicle surrounded by connective tissue, round cell infiltration and fat cells.

the sacrum in the midline between the buttocks about 2 inches (5 cm.) posterior to the anal verge; or the process may extend down on either side of the buttocks.

Pilonidal sinus must not be confused with fistula in ano, ischiorectal abscess, simple furuncle, sebaceous cyst, tuberculosis, osteomyelitis, lipoma, inflammation of the congenital tumors, anthrax or actinomycosis.

INCIDENCE

The pilonidal sinus is common and occurs in early adult life. In conformity with the experience of others, the ages of the patients in our series of cases ranged from 18 to 51 years (see table). Men predom-

14. Brams, J.: *Radiology* 8:248, 1927.

inated over women in a ratio of 8 to 3. There were no Negro patients. The majority of the patients were of the obese hirsute type. One patient was tuberculous, 1 was paretic and 1 was convalescent after encephalitis.

SYMPTOMS

The early dimple stage is usually symptomless. The acute stage is characterized by swelling and by severe pain over the sacrococcygeal region and over the lower part of the back. The pain radiates down one or both thighs or to the rectum, is rather constant, varies in intensity and is aggravated by sitting, by walking and sometimes by defecating. There may be fever, chills and malaise. In the chronic stage the chief complaint is a dull aching pain in the involved region on walking or sitting, a discharge of pus which often causes itching, an odor and the presence of hair in the orifice leading into the tract.

PROGNOSIS

Recurrence appears to be the bane of almost every radical procedure employed in the treatment of this disease. The condition frequently

Distribution of Patients According to Age and Sex

Age.....	18	21	23	24	26	34	39	41	40	51
Number of patients.....	2	1	1	1	1	1	1	1	1	1
Sex.....	F	F	M	M	M	M	M	M	M	M

demands a second operation, and occasionally, repeated surgical intervention is necessary. A perusal of some of the figures is interesting. Weinstein,¹⁵ Ferguson,¹⁶ Thomason¹⁷ and Rogers and Hall (third series¹³) reported no recurrences; Colp,¹⁸ Ottenheimer,¹⁹ Smiley,²⁰ Lynch²¹ and others did not mention the exact percentage of recurrences in their series of cases, alluding only to their frequency. However, Worter²² reported 15 per cent, Owen²³ 5 per cent, Breidenbach and Wilson⁸ an average of 35 per cent, Glenn²⁴ 17 per cent, Cattell and Stoller²⁵ about 22.5 per cent and Stone⁷ 5 to 8 per cent when the opera-

15. Weinstein, M.: *Ann. Surg.* **97**:80, 1933.

16. Ferguson, L. K.: *Ann. Surg.* **101**:469, 1935.

17. Thomason, T. H.: *Ann. Surg.* **100**:585, 1934.

18. Colp, R.: *S. Clin. North America* **9**:695, 1929.

19. Ottenheimer, E. J.: *Am. J. Surg.* **21**:120, 1933.

20. Smiley, K. E.: *Am. J. Surg.* **27**:298, 1935.

21. Lynch, J. H.: *Nebraska M. J.* **19**:20, 1924.

22. Worter, C. W.: *Tr. Am. Proct. Soc.* **29**:13, 1929.

23. Owen, H. R.: *S. Clin. North America* **14**:117, 1934.

24. Glenn, F.: *New England J. Med.* **207**:544, 1932.

25. Cattell, R. B., and Stoller, L. W.: *New England J. Med.* **206**:110, 1932.

tion was in good hands and up to 35 per cent in other cases. Rogers and Hall (first and second series¹³) in a comprehensive study in which they found 19 per cent recurrences in original cases and 75 per cent in acute and recurrent ones concluded that one must avoid radical excision to assure satisfactory results. They depended on the removal of all diseased tissue present at the time of operation and present in the wound during the process of healing.

Residual symptoms in the scar after radical excision have also been mentioned. Lahey²⁶ recommended the pedicle flap to obviate this undesirable sequela. Rogers and Hall¹³ reported residual symptoms, such as pain, discomfort and numbness, in 39 per cent of patients operated on.

In our series of 11 cases of pilonidal sinus observed during a period of four years there was neither a recurrence of the sinus after the operation nor a complaint of any untoward scar symptoms.

TREATMENT

Three types of operation are employed for the eradication of this lesion:

1. Nonambulant radical excision. This, of course, is the method of choice for the majority of surgeons. There are various modifications of the same procedure, such as primary closure, partial closure, open packing and a combination of these.

2. Ambulant radical excision. This method appears to be an improvement and is certainly worthy of favorable comment. Two different procedures have been employed, with a striking resemblance in the manner of approach. There is a deliberate attempt to conserve skin and at the same time to excise extensively the underlying tissue. This in our opinion is an important and logical course to pursue. Primary suture has been employed by Ferguson¹⁶ in selected cases in which the patient was well prepared, with only 1 recurrence in 21 cases. This single recurrence was observed in a patient in whom the acuteness of the condition was regarded by Ferguson as a contraindication to immediate intervention. The cautery method described by Stanton has been employed by Rogers and Hall¹³ in a series of 50 cases, with no recurrences and excellent results.

3. Ambulant simple incision followed by repeated applications of a sclerosing solution. This is, in our opinion, the most satisfactory and effective means available for the eradication of this annoying condition. It is entirely ambulant, is painless, requires no sedation and leads to no recurrence or residual symptoms. Even the most compli-

26. Lahey, F. H.: *Surg., Gynec. & Obst.* 48:109, 1929.

cated sinus, consisting of many lateral tracts and pouches, lends itself to this treatment. There is an immediate relief from pain and a gradually increasing freedom from odor and discharge. The fact that infection is immediately checked or entirely eliminated after the first few applications of the solution is of inestimable value. This observation seems to refute the generally accepted theory that the proximity of the anus to the operative wound is the cause of persistent infection. This condition is probably due to the retention of infected tissue in the wound.

Most of the tract is usually obliterated, and the remaining portion is free of infection and completely fixed after a few treatments. If incomplete healing does occur, further incision and excision may be accomplished ambulantly without fear of recurrence or of any other untoward effect. We resorted to subsequent incisions when unexpected bridging had occurred or when a tract had been overlooked, and in some cases to the excision of portions of the lesion for microscopic study, without in any way retarding the healing progress of the wound.

The preparation used is a modification of Carnoy's solution, consisting of absolute alcohol 6 cc., chloroform 3 cc., glacial acetic acid 1 cc. and ferric chloride 1 Gm. This solution was described and suggested by Cutler and Zollinger²⁷ in 1933.

Despite condemnation by Colp¹⁸ and the unfortunate experience of Rogers and Hall¹³ in 1 case, we feel that the method is sound surgically and is superior to all other methods proposed. Smiley²⁰ reported success in the treatment of the condition in 3 simple cases over a period of six months; we have successfully treated it in 11 cases, not selected, over a period of four years. In 8 of these the treatment was given in the office; in 1 it was given in a tuberculosis sanatorium, and in the other 2 it was given in a state hospital for the insane.

Ambulant nonoperative treatment by galvanic current was employed with success in 1 case by Maillard.²⁸ Crookall²⁹ resorted to the use of silver nitrate flakes and a silver nitrate stick in 2 cases with satisfactory results. The treatment, however, was cumbersome, and the patient complained of severe pain and hemorrhage.

TECHNIC OF THE SCLEROSING TREATMENT

This method of treatment is employed exclusively in all cases of pilonidal sinus, whether the condition is acute or chronic and whether it is simple or complicated.

27. Cutler, E. C., and Zollinger, R.: *Am. J. Surg.* **19**:411, 1933.

28. Maillard, E. R.: *Nonsurgical Treatment of Pilonidal Cyst*, J. A. M. A. **93**:1383 (Nov. 2) 1929.

29. Crookall, A.: *Tr. Am. Proct. Soc.* **28**:32, 1928.

Either iodized poppyseed oil or paste of bismuth N. F. is usually injected into the main orifice, and a roentgenogram is taken to determine the extent of the lesion. Bismuth paste seems to be the more satisfactory, especially if there is more than one orifice. The secondary orifices should be sutured or plugged with the finger when the paste is being forced into the tract. It is well to note here that we do not use any dye to delineate the tracts. In our opinion methylene blue or any other delineating agent is entirely unnecessary, but if one wishes to outline the tracts bismuth paste will admirably serve the purpose and because of its viscosity will not penetrate normal tissue.

The patient is then placed in the prone position again, and the region is prepared in the usual manner for the operation. The skin is infiltrated with a 2 per cent solution of procaine hydrochloride along the midline and if necessary to one side or the other for a short distance to facilitate the incision and the exposure of lateral tracts. (In some cases we resorted to block anesthesia, which is also eminently satisfactory.) The type of incision may be the T shaped, the crucial or the vertical, depending entirely on the extent of the lesion. The wound is not guttered, but it is extremely important to uncover all tracts. The wound is then tightly packed with iodoform gauze (treated with petrolatum, if desired), care being taken to fill every tract, pouch and crevice. The patient is then discharged. Irrigation of the wound as suggested by Cutler and Zollinger²² is entirely omitted.

In two or three days after the initial incision the sclerosing treatment is instituted. The pack is removed carefully and gently; the table is tilted so as to lower the upper half of the body to an angle of about 60 degrees, and the wound is completely filled with a 2 per cent solution of butyn for five minutes (anesthesia). The skin around the wound is covered with petrolatum or a zinc oxide ointment. The butyn solution is then wiped up by means of cotton pledgets or gauze, and the wound is filled completely with a modified Carnoy solution, which is allowed to remain for five or ten minutes (usually only five minutes). This tans the tissue and acts as an effective hemostatic. The excess solution is then removed, and the wound is packed carefully, as before, with iodoform gauze. A proper dressing is applied. This process is repeated every three or four days until complete healing ensues.

It is imperative to prevent bridging over by frequently and carefully testing the forming scar for any areas of defective healing. We found it necessary occasionally to incise two or three times to insure the formation of a solid scar. Light curettage may be necessary, but if it is too vigorously done or too often repeated it may retard the healing of the wound.

The most satisfactory dressing (fig. 3), in our opinion, is applied as follows: The packed wound is covered with a few layers of sterile

gauze about 2 inches (5 cm.) square. Strips of adhesive plaster 1 inch (2.5 cm.) wide and 4 inches (10 cm.) long are so placed that one half of the width covers the dressing and the other half the skin. Four strips are used for the entire dressing.



Fig. 3.—Suitable dressing, simple and sufficient for the absorption of all discharges. It is comfortable, and the patient's underclothing is seldom soiled.



Fig. 4.—Thin, linear white scar left after healing. In every case the wound healed completely. The scar is firm, movable and free from residual symptoms.

The bleeding in the cases in our series was insignificant and was completely controlled by the hemostatic properties of the solution and by packing, which is of prime importance in this procedure. The post-operative pain was trivial. A few patients complained of some discomfort for an hour or two after the treatment, but no patient complained of disabling pain. A remarkable feature was the total absence of purulent discharge in most cases after the first application of the sclerosing

solution. A persistent discharge or odor, which disappeared after a few treatments, was noted in 2 cases. There was rapid filling in of healthy granulation tissue. The minimum time required for complete healing was about four weeks, and the maximum was ten weeks. The number of treatments varied from a minimum of eight to a maximum of twenty-two. The total average number of treatments after the initial incision was 16.2. There was absolutely no hospitalization, no loss of time from work or pleasure and no recurrence. In every instance a firm, simple, freely movable incisional scar formed, completely free from residual symptoms.

REPORT OF CASES

We submit a brief abstract of 4 of the 11 cases in which the condition was treated and observed during a period of four years and complete and permanent cure resulted.

CASE 1.—H. K., a man aged 23, had a history of trauma six months prior to the formation of an abscess which ruptured spontaneously and drained continuously for a period of two years.

The patient was underweight and tuberculous. He was not hirsute. No previous treatment had been given. He complained of discharge, of odor and of pain and discomfort when sitting or walking. Examination disclosed a single skin-lined orifice in the midline, leading into a tract about 4 cm. long. Purulent discharge and odor were present, but there was no hair. A primary vertical incision and two subsequent incisions of the tract were made, and nineteen applications of the solution were administered during a period of sixty-nine days (July 10 to Sept. 17, 1933). There was no discharge or odor, and very little pain was noticed after the first treatment. There was a freely movable scar. There were no complaints of residual symptoms. No recurrence was observed.

CASE 2.—C. F., a man aged 24, had a history of trauma seven years prior to the onset of an acute abscess. The abscess was "lanced" and treated as a "carbuncle" three times between 1927 and 1929.

The patient was obese and hairy. He complained of periodic discharge of pus, of odor, of pain, of discomfort when sitting or walking and of the presence of loose strands of hair extruding from the opening in the wound. Examination disclosed a single skin-lined discharging orifice in the midline and two secondary orifices about 2 cm. above, one to the right and one to the left. A tuft of hair was seen. Swelling and discoloration were present. There was a tract about 5 cm. long. A primary crucial incision followed by seventeen applications of the solution during a period of sixty-one days (June 24 to Aug. 25, 1934) gave excellent results. There was no discharge, no odor and no pain after the first four treatments. There was a deep saddle-like scar, freely movable and entirely symptomless. No recurrence was observed.

CASE 3.—H. K., a man aged 34, had no previous history of trauma. He suddenly noticed a "boil" which ruptured spontaneously and drained periodically for a period of two years. No previous treatment had been received.

The patient was obese and hairy. He complained of pain, discomfort on sitting or walking and of periodic purulent discharge. A discharging skin-lined orifice was found in the midline, and a secondary orifice was seen about 3 cm. above and to the left. No hair was noticed. A primary vertical incision was made fol-

lowed by nine applications of the solution over a period of thirty days (Aug. 4 to Sept. 4, 1935). The patient had some discomfort for periods varying from one to three hours following the first two or three treatments, but no discomfort was felt afterward. The results were excellent; no pain, discharge or odor was present after the third treatment. No residual symptoms were noticed in the freely movable scar. There was no recurrence.

CASE 4.—G. C., a woman aged 18, had a history of trauma four years prior to the onset of an acute abscess which ruptured spontaneously one year prior to this treatment. No previous treatment had been received.

The patient was well developed but not obese. She complained of periodic purulent discharge and of pain and discomfort when sitting or walking. Examination disclosed two discharging orifices, one (skin lined) in the midline and the other about 4 cm. to the right. The tract measured about 5 cm. in length. A primary vertical incision was made with a lateral incision to the right, exposing the tract and a pouch. No subsequent incisions were made. Eighteen applications of the sclerosing solution were given over a period of seventy-six days (Oct. 7 to Dec. 23, 1935). The results were excellent. The patient had no pain after the first treatment; there was no discharge and no odor. There was a freely movable scar. No residual symptoms were observed.

SUMMARY AND CONCLUSIONS

A brief review is presented of the essential features of the subject of pilonidal sinus and of its controversial phases.

A thorough study of the anus, the rectum and the colon of every patient is imperative before a diagnosis of pilonidal sinus is made and the sclerosing treatment instituted.

Eleven patients afflicted with pilonidal sinus were treated with simple incision and the application of a sclerosing solution during the past four years.

Every patient was ambulant during the entire course of treatment, and no hospitalization, loss of time or extraordinary expenditure was required.

The treatment was painless except for discomfort experienced by the patient for a very short period after the application of the solution in the early stages of the treatment.

A very small linear and movable scar formed, free from all residual symptoms.

There was no recurrence in any of the cases in this series.

Pilonidal sinus is, in our opinion, particularly amenable to the sclerosing treatment, and the essential requirements are simple but must be judiciously fulfilled to assure success.

We are convinced that this procedure for the eradication of this annoying lesion is vastly superior to any other heretofore employed.

The solution of butyn was supplied by the Abbott Laboratories, North Chicago, Ill.

A NEW APPARATUS FOR MAINTAINING HOT COMPRESSES AT CONSTANT TEMPERATURE

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That hot wet dressings are definitely of value in the treatment of certain conditions is an unquestioned fact. Also it is readily acknowledged that the efficiency of the compress is in direct ratio to the constancy of its temperature. How to maintain hot wet compresses at constant temperature has been the problem for solution. While making daily rounds of the wards I have found compresses too cold or, on occasions, have encountered evidence of their having been applied too hot. It was this circumstance that prompted me in 1933 to start experimental work on the subject. The inadequacy of the present methods is experienced in all hospitals, large or small, and this experience is no reflection on a busy nursing staff.

Five objectives for which one should strive in using a hot compress were first listed as follows:

1. Constant or nearly constant temperature at the surface of the skin.
2. A simple method for keeping the compress moist.
3. A means of checking the temperature at the surface of the skin at all times.
4. Safety with minimum attention from the nurse or attendant.
5. Comfort for the patient.

As 108 to 110 F. was the generally accepted temperature at which hot compresses should be applied, this temperature was first assumed as the objective. An ordinary electric heating pad was obtained and its thermostats set at 120 F. It was felt that 10 to 12 degrees would approximately compensate for heat lost by the absorptive action of the body, by radiation or by the insulation of the cloth compress between the heating unit and the skin. This heating unit was then covered with rubber to make it waterproof.

Experiments with different fabrics soon showed that outing flannel was best suited for the cloth part of the compress, because of its ability

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to absorb solutions. A standard thickness was deemed necessary for all cloth compresses used. Four ply flannel compresses were then constructed because this thickness seemed to be approximately correct.

The heating unit was preheated by plugging it into a socket and waiting until it attained its maximum temperature—120 F. Then the cutting flannel compress was dipped into a 5 per cent solution of magnesium sulfate at 112 F. and placed on the skin with a thermomenter between it and the skin. The heating unit was then superimposed and fastened in place by ties. I was somewhat surprised to note that in several repetitions of the experiment the temperature at the surface of the skin persistently dropped to 100 F. or less in ten to fifteen minutes. Consideration was then given to the physiologic factors regulating the heat in the body. It became evident that more heat was necessary in the heating unit to overcome the refrigerating action of the body. Therefore, the thermostats were gradually "set up" in an effort to attain a *mass* of heat which when liberated from the resistance coil in the heating unit would be sufficient to overcome the absorption of heat by the body and to keep the compress at the surface of the skin at 108 to 110 F. This objective was finally accomplished in the case of a certain normal person, at one particular part of the body, when the thermostats were set at approximately 170 F. That most of the loss of heat was not due to radiation was demonstrated when the apparatus was placed on an inanimate object, such as the top of a table. It was noticed that the temperature between the flannel compress and the top of the table soon approached 170 F.

Several heating units were then built and experiments made on different parts of the body in the same person and on corresponding surfaces of the body in different persons. It soon became evident that no two persons and no two parts of the body in the same person absorb the same amount of heat. The nature of the pathologic process also was found to be a definite factor in determining how much heat would be absorbed. For normal persons the amount of heat necessary to obtain a constant temperature at the surface of the skin seemed to depend on the following factors primarily:

1. The size of the body and its blood volume.
2. The temperature and humidity of the room.
3. The vascularity of the specific part of the body being heated and of the adjacent structures.
4. The pressure of the compress against the heated part.

Because of these factors it was concluded that in order to produce the desired temperature the mass of heat applied to any given area of the body must be readily alterable within wide limits. Therefore, a

rheostat of sufficient potential resistance to allow for these variable factors was introduced into the system.

Automatic thermostats to control the heat in conformity with this requirement were considered but given up. For reasons already mentioned, the control would have to be at the surface of the skin. This was felt to be mechanically and economically impracticable even if such a control could be developed.

At this stage of investigation a definite stumbling block was encountered, namely, the discovery of hot spots in the compresses. These resulted in a superficial burn in 1 case. They were easily located experimentally and were much more noticeable in the double compress to be described later. In these double compresses in which the hand, with the fingers spread, was inserted between two units, the temperature between the fingers soon built up to approach that in the resistance coil above and beneath it. The reason for this was simply that in the areas of the cloth compress not in contact with the skin there was no absorbing mechanism to carry a part of the heat away. If the hand was moved so that these areas came in contact with the skin, the latter was then exposed to increased temperature, often sufficient to cause disintegration of the epithelium. The same difficulty was encountered to a lesser degree with the single compresses because of increase in the mass of wire at the turning points of the wiring. Furthermore, a peripheral part of the applied compress often became raised from the corresponding area of the skin with a resultant rise in its temperature.

Various methods for overcoming this difficulty were the object of experiment for over a year. Finally it was found that when the heating unit was wired in the design of an involute coil (fig. 1) no hot spots developed. The involute coil concentrated the *mass of heat* liberated at the center of the compress with gradual diminution toward the periphery, although the *temperature* of the resistance wire was the same throughout. When the compress was in use, the thermometer lying at the surface of the skin directly beneath the area of the greatest concentration of heat gave an accurate reading of the maximum temperature and eliminated all danger.

The four ply flannel compress had been previously found to remain moist though heated for from eight to ten hours. This compress was fitted with a cloth sleeve to contain the thermometer on the side next to the surface of the skin. This measure was adopted for two reasons: 1. The thermometer itself when in direct apposition with the skin provided an excellent insulator to the portion of the skin with which it was in contact. 2. By means of the sleeve the thermometer was held in place so that its bulb lay at the point in the system where the heat was most concentrated—viz., the center. Of course the cloth sleeve was somewhat of an insulator itself, but when only one thickness of cloth was

used there was little difference between the temperature recorded by the thermometer and the temperature at the surface of the skin.

Several changes have been found necessary since the first apparatus was completed. Ordinary thermometers were at first used, but changes in temperature were noted during the process of extracting the thermometer and reading it. Therefore, special thermometers were designed,

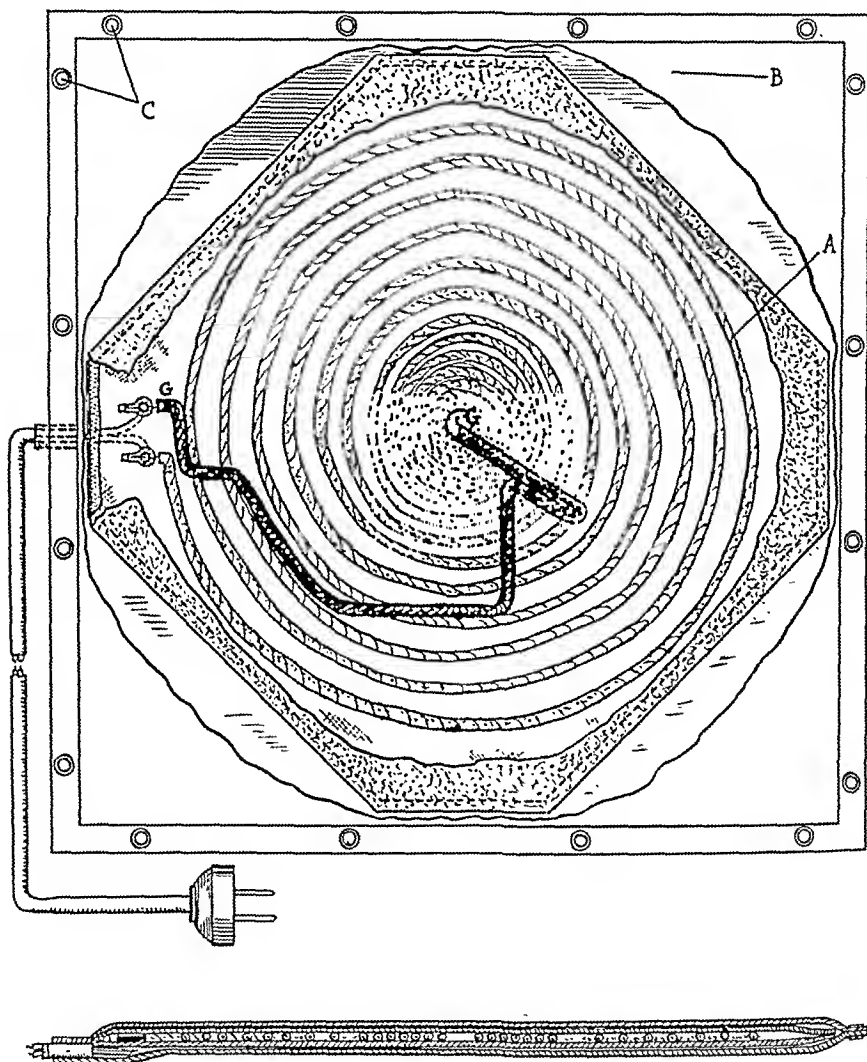


Fig. 1.—Heating unit wired in the design of an involute coil.

calibrated in such a manner that they could be read without removal from the sleeve. These thermometers revealed at a glance the temperature at the surface of the skin in the region of the greatest concentration of heat. They were metal jacketed to insure against breakage. However, the metal jackets were later given up because of the increased pressure due to their weight and because of their tendency to conduct

and concentrate heat. This tendency in 1 case was responsible for a slight burn, which, though it occurred in an area which was comparatively avascular because of previous trauma, revealed the necessity for removal of this causative factor. Another important change was the separating by heavy insulation of the wire leading out of the system G-G, (fig. 1) from the rest of the coil.

The following is a description of the perfected apparatus: Figure 1 shows the wiring of the heating unit. This, as is readily noted, is in the design of an involute coil. The heat liberated is concentrated at the center and diminishes at the periphery, although the temperature of the wire is constant throughout. In operation the central part lies directly over the center of the outing flannel compress, where the bulb of the thermometer is placed. This wiring is labeled *A*. *B* is the water-proof covering, of such material and construction that it will tolerate heat to 200 F. *C* represents the grommets along the edges of the covering for the insertion of ties to hold the compress in place. If for any reason this covering should be perforated during operation and the solution allowed to surround the wire coil, the latter will not cause any appreciable shock to the patient because of the low amperage used.

Figure 2 shows the single outing flannel compress with the thermometer, *D*, inserted in its sleeve, *E*, on the surface of the skin or wound. This compress will absorb a relatively large amount of solution and will remain moist though heated for eight to ten hours. Figure 3 shows the double outing flannel compress for the hand. The same principle may be used for other parts, such as the forearm or the elbow. However, when a double compress is used, two heating coils, with two independent rheostats (shown mounted in the same rheostat box in the photographs), and two thermometers are required.

The reason for this requirement is that because of the pressure on the lower coil exerted by the weight of the hand or other part less heat is necessary in that unit to maintain the desired temperature at the surface of the skin. The cloth compresses are easily autoclaved and applied sterile. Figure 4 shows the double and the single unit in cross section. Figure 5 shows the single rheostat. The photographs in figures 6 and 7, show the single, large and small, and the double unit in operation.

Many attempts have previously been made by others to construct such an apparatus. These have, so far as I know, been given up because of burns in certain cases. The combined physiologic and mechanical difficulties responsible for these burns have, I believe, been overcome by the combination of the involute coil, the cloth compress of standard thickness, the sleeve for the thermometer, the thermometer which tells the temperature at the surface of the skin or wound at the point where

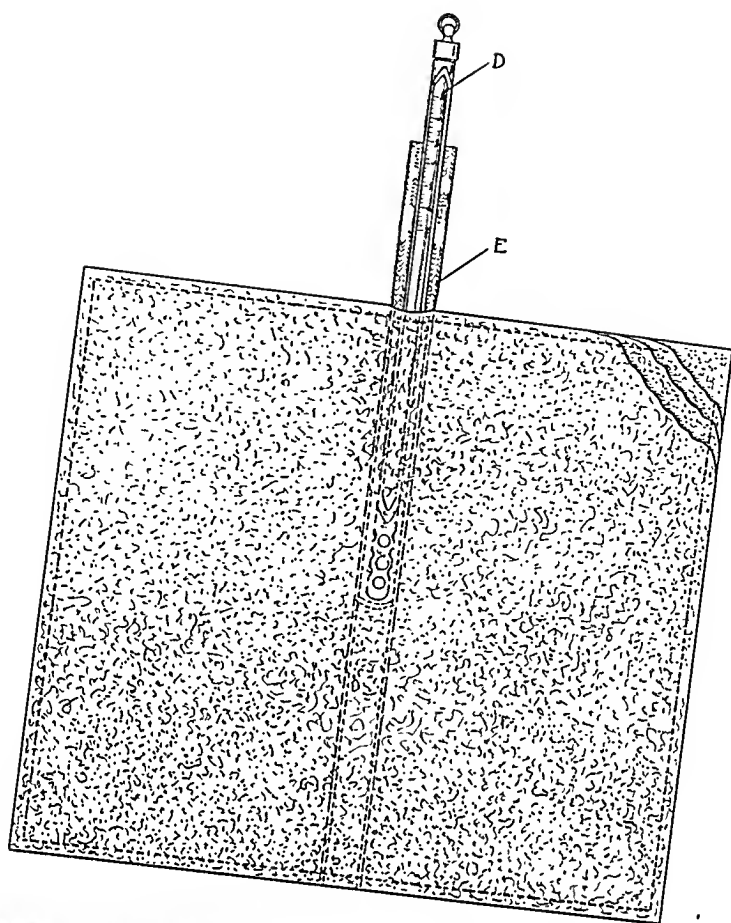


Fig. 2.—Single outing flannel compress with the thermometer inserted in its sleeve.

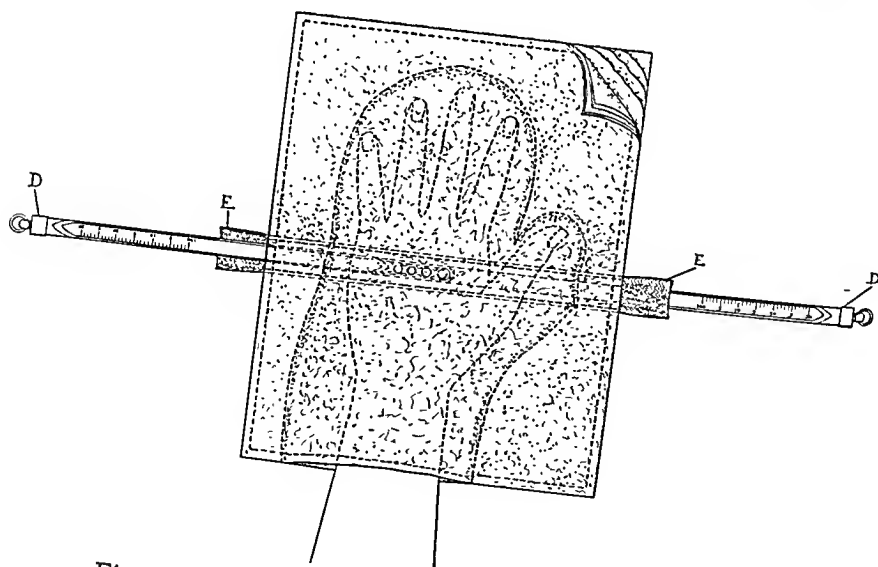


Fig. 3.—Double outing flannel compress for the hand.

the mass of heat is the greatest and the rheostat which allows the quantity of heat to be altered. I propose that the apparatus be made in various sizes suitable for application to different parts of the body.

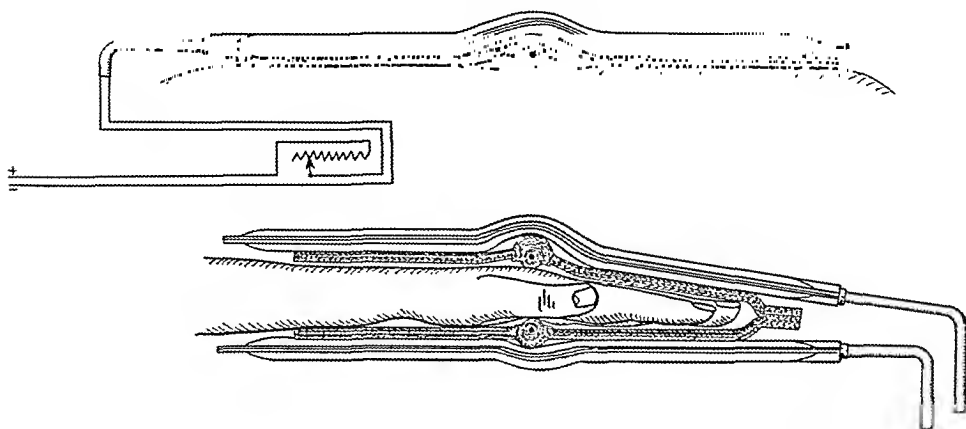


Fig. 4.—Double and single unit in cross section.

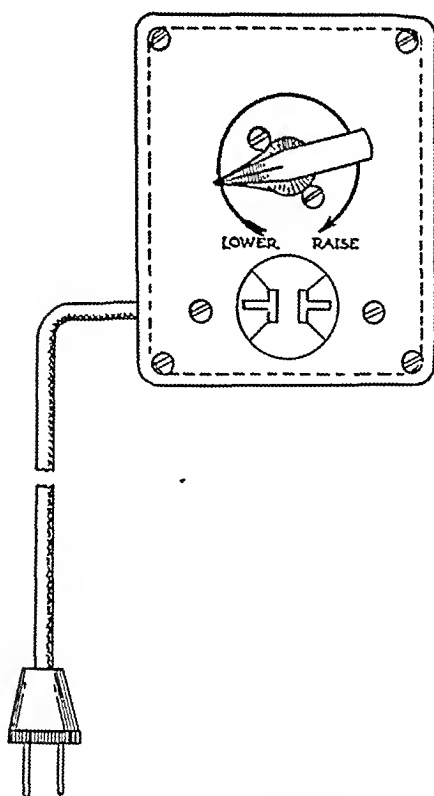


Fig. 5.—Single rheostat.

Various solutions have been used for moistening the compress. Magnesium sulfate in a 5 to 10 per cent solution has been the medicament of choice in most cases of cellulitis. However, for cellulitis about



Fig. 6.—Large and small single unit in operation.



Fig. 7.—Double unit in operation.

the eye, boric acid was used. This solution was used also for varicose ulcers. On infected wounds (open) a mild germicide, such as diluted solution of sodium hypochlorite U.S.P. or azochloramine, has been the solution of choice. Physiologic solution of sodium chloride has been used after grafting skin.

CLINICAL EXPERIENCE

During the last four years approximately 30 patients have been treated with the apparatus in its various stages of development. The experience with these patients seems to indicate that properly controlled wet heat has more therapeutic value than may have been previously supposed. Excellent results have been obtained in treating chronically infected wounds. For such wounds the compress has been utilized in two ways: (1) to clear up the infection and to stimulate fresh, clean granulations, and (2) to stimulate the "taking" of subsequent skin grafts to the wound. Varicose ulcers of long duration appear to respond equally well to this form of treatment. Superficial pyogenic infections seem to become localized and heal more quickly than when other methods alone are used.

The temperature at which the compresses should be maintained appears to vary with the pathologic conditions. In cases of acute pyogenic cellulitis 108 to 112 F. seems optimum; in cases of chronic cellulitis, such as that associated with osteomyelitis, lower temperatures for longer periods are advisable (104 to 108 F.). In cases of the latter type I have kept the compresses on constantly for as long as thirty days before skin grafting. Varicose ulcers require about the same temperature for approximately seven or eight days before skin grafting. Skin grafts respond better at still lower temperatures (102 to 104 F.). More can be said as to the length of time for which the compress should be kept in place and the temperature advisable for various conditions after more patients have been treated.

The exact physiologicobacteriochemical reaction to the local application of wet heat is not clearly understood. It offers an interesting subject for study. An attempt may be made to experiment further on this reaction, and if so it will be reported, together with a series of cases, at a later date.

This apparatus in no way precludes the necessity for keen surgical judgment, particularly in cases of acute streptococcic cellulitis. Furthermore, it should be used only under the close supervision of the physician. It is not offered in competition with other forms of treatment but rather as a means of supplementing existing methods of therapy.

BILATERAL COLLAPSE THERAPY IN THE TREATMENT OF PULMONARY TUBERCULOSIS

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SECAUCUS, N. J.

Although bilateral artificial pneumothorax was introduced about a quarter of a century ago, there still exist wide differences of opinion as to the value of this form of therapy in the treatment of pulmonary tuberculosis and as to the type of condition to be selected for its use. When bilateral application of such a measure as phrenicotomy or thoracoplasty or a combination of these procedures with or without pneumothorax is considered, the variation in opinion is still wider.

In view of these circumstances it is felt that the addition of another paper to the literature, recording my experience in a comparatively

TABLE 1.—*Bilateral Pneumothorax—Availability of Pleural Space*

Type of Space	Number of Cases
Bilateral space.....	152
Unilateral space.....	49
No space.....	10
Total number of cases.....	211

large series of cases observed over a period as long as five years, will add clarity to the subject. This study comprises, in all, 211 cases in which pneumothorax was attempted bilaterally, with results as regards the availability of a pleural space as revealed in table 1. As will be shown later, some of the patients for whom the pneumothorax was abandoned or unobtainable on one or both sides were subjected to the more radical surgical measures.

Before going into detail as to the fate of the 211 patients, I should like to make clear the basis on which the selection of patients for collapse therapy was made. Having discussed this subject thoroughly elsewhere,¹ I wish merely to state, first, that for no patient in this group was collapse therapy used unless cavitation was present and, second, that artificial

From the Hudson County Tuberculosis Hospital and Sanatorium.

Read at the Annual Meeting of the American Academy of Tuberculosis Physicians, Atlantic City, N. J., June 8, 1937.

1. Potter, B. P.: Modern Concepts on the Collapse Therapy of Tuberculous Pulmonary Cavities, *Am. Rev. Tuberc.* 31:499, 1935.

pneumothorax was the first measure of choice. Interestingly, cavities of moderate or large size were present bilaterally on the patients' admission to the hospital in the vast majority of instances; in the remainder, necrosis took place in the contralateral lung after a unilateral effective collapse had existed for some time. Still a further point of interest is the fact that pulmonary tuberculosis in 95 per cent of the patients was classed as far advanced according to the standards of the National Tuberculosis Association.

BILATERAL PNEUMOTHORAX

A pleural space was encountered bilaterally in 152 of the 211 cases. While this incidence may appear high, especially when one considers the stage in which the disease was treated, it is nevertheless closely similar to that found in 520 cases of attempted unilateral pneumothorax. As will be seen later, this close parallelism between bilateral and unilateral pneumothorax exhibits itself again when the question of the number of effective collapses and the complications are taken into account.

TABLE 2.—*Type of Pneumothorax in 152 Cases of Bilateral Pneumothorax*

Simultaneous.....	119
Alternating.....	33

It is important to know the type of pneumothorax under consideration when the problems of bilateral collapse are discussed because, for obvious reasons, an alternating pneumothorax presents, with few exceptions, difficulties no different from those encountered in the unilateral form. As is shown in table 2, and as was to be expected from the type of cases selected, simultaneous pneumothorax is the predominant feature of this study.

While pneumothorax was induced on either one side or the other immediately or within two months after the patient's admission to the hospital, the interval between bilateralization averaged ten months but was as low as one month in a few instances. In retrospect I feel that this average interval could have been reduced to eight months or possibly even less, but I lean strongly toward a reasonably liberal period of observation between the induction of the first pneumothorax and that of the second, for the following reasons: In the first place, it is desirable that an effective collapse be either present or reasonably certain of occurrence without further intervention before one attacks the contralateral lung; for it has been my experience (as well as that of others) that pneumonolysis, if it should become necessary, may be hazardous in the presence of a bilateral pneumothorax. In the second place, I

have found that varying portions of relatively uninvolved lung may have to be sacrificed during the establishment of satisfactory pneumothorax. However, such sacrifice should not be continued once an effective collapse is achieved, as optimum functional respiratory integrity should be restored by permitting the reexpansion of the uninvolved portions before contralateral collapse is induced. Under such conditions the patient is able to withstand with little or no discomfort any further reduction of lung volume that may be entailed. Finally, as the more involved lung becomes effectively collapsed, the lesion on the opposite side may become controlled, and thus collapse may be obviated.

Of course, one is often compelled to deviate from this ideal practice either because of progression of the lesion in the uncollapsed lung or because of the development of pleurisy, threatening obliteration of the corresponding pleural space. When it is further remembered that, in spite of the presence of offending adhesions in 60 to 70 per cent of the cases and of the fact that their severance was indicated in only 4 per cent, it becomes evident that the second pneumothorax in many instances was induced while the first was still ineffective.

Another point for consideration concerns the side to be selected for the first pneumothorax. A review of the literature on bilateral pneumothorax indicates general agreement that the lung showing the more active lesion should be favored initially. While on the whole this criterion is useful, there are cases of a bilateral process in which the difference in degree of activity is difficult to determine, especially if there are no comparative roentgenograms, as is often the case. Furthermore, with most of the patients with simultaneous pneumothorax in the group under present consideration the problem centered about the cavities in the lungs, involving such questions as their size, their location and the character of the pericavernous infiltrate. Another factor is a history of roentgenologic evidence of recent pleural involvement, which warrants the early induction of pneumothorax to obviate the loss of a possible free pleural space. It is obvious, therefore, that the question of which lung is to be chosen for initial collapse will depend on conclusions drawn after due consideration has been given to the factors just cited.

As for the actual technic, my experience may be cited with respect to several controversial issues. It is generally conceded that a pneumothorax should not be established bilaterally at the same sitting, on the same day or even in the same week. It is conceivable that because of profuse uncontrolled hemorrhage of undeterminable pulmonary origin bilateral collapse may become urgent, but this must be a very rare occurrence, as evidenced by the fact that I have not encountered it in a single instance.

After bilateralization of the pneumothorax, the question arises whether refills should be given at the same sitting. While the patient is in the hospital and is available for frequent observation or treatment, refills may be confined to one side at a time. Once he has been discharged, however, I do not hesitate to insufflate both sides at the same sitting. In fact, it is generally preferable to do so, in order to assure the maintenance of nearly equal intrapleural pressures. In several instances in which this point was overlooked, the patients noticed various symptoms, such as wheezing in the chest, irritating dry cough or shortness of breath, all of which disappeared with equalization of the intrapleural pressures and the return of the mediastinal structures, if displaced, to the midline. As will be shown later, no untoward complications have been noted from this practice.

The other features of the technic differ in no respect from those that apply to unilateral pneumothorax. I wish to stress, however, that it is essential that the collapse be confined as far as is possible to the diseased portions of the lungs. This can be best accomplished during the patient's residence in the hospital by refills of small quantities (150 to 250 cc.) of air three times a week, and after discharge by weekly refills of not more than 350 cc. of air.

The adequacy of any surgical measure in the arrest or "cure" of pulmonary tuberculosis must be judged also by its capacity to return the patient to a state of health compatible with social usefulness. Mere obliteration of the cavity and prolongation of life with the patient left in a state of invalidism is not in my opinion a satisfactory result. Although it might be expected that bilateral collapse would place greater limitations on the patient's useful existence, my experience reveals that this is not actually so.

As may be seen from table 3, 45, or 79 per cent, of the 57 patients in whom an effective bilateral pneumothorax was achieved are working, able to work or ambulatory; and these results closely parallel those obtained in a much larger series of cases of unilateral pneumothorax.

When the frequency of the effectiveness of bilateral pneumothorax is compared with that of the same procedure in cases of unilateral cavitation, close similarity again demonstrates itself. Thus, in the series represented in table 3 the collapse became effective bilaterally by pneumothorax in 57 of the 152 cases, showing an incidence of 37 per cent as against 38 per cent of instances of closure of the cavity in another group of 398 patients in whom the lesion presented a problem of unilateral collapse therapy.

The complications differ in no respect from those encountered with unilateral pneumothorax. Differences of opinion have arisen only as regards their comparative frequency. So far as pleural effusions are

concerned, I have had an incidence of 50 per cent in cases of bilateral pneumothorax as against 34 per cent with unilateral pneumothorax. However, the incidence of effusion per pneumothorax was only 25 per cent. The fluid became empyematous in about an equal number of instances (8 per cent). Superimposed spontaneous pneumothorax of clinical significance was noted in only 4 patients, all of whom responded favorably to underwater drainage.

Before concluding the subject of bilateral pneumothorax, it may be of interest to inquire about the anatomic status of the lungs which were permitted to reexpand after an effective collapse had existed and

TABLE 3.—*Clinical Status of 152 Patients in Whom a Bilateral Pleural Space Was Found**

Groups	Working or Able to Work	Ambu- lant	Im- proved	Unim- proved	Dead	Total
Bilateral effective pneumothorax.....	28	17	5	3	4	57†
Unilateral effective pneumothorax; con- tralateral pneumothorax abandoned..	2	9	4	2	0	17
Bilateral pneumothorax abandoned.....	0	5	0	21	50	76

* The remaining 2 patients with original bilateral pleural space are included in table 5.

† Collapse was made effective by pneumonolysis in 4 cases and by supplementary phrenicotomy in 1.

TABLE 4.—*Anatomic Status of Reexpanded Lungs*

Both Lungs Reinflated			One Lung Reinflated		
Bilateral Closed Lesion	Unilateral Closed Lesion	Total Number of Cases	Closed Lesion	Open Lesion	Total Number of Cases
13*	4	17	9	0	9

* In 2 cases collapse was made effective on one side by thoracoplasty and thoracoplasty plus phrenicotomy, respectively, after an ineffective pneumothorax had been abandoned.

of the condition of which a follow-up is available for periods varying from several months to four years. The data in the 26 cases analyzed in table 4 are drawn from the patients comprising the first two groups in table 3. It is evident that bilateral pneumothorax if effective serves not only as an immediate control measure but also eventually leads to arrest of the disease. What is even more impressive is the fact that the incidence of residual closed lesions after reexpansion in this group closely parallels that found in my patients with unilateral pneumothorax.

COMBINED COLLAPSE THERAPY OTHER THAN EXCLUSIVE PNEUMOTHORAX

When obliteration of bilateral cavitation is sought by measures other than exclusive pneumothorax, the complexity of the problem is increased proportionately as the more radical surgical procedures are utilized in

the combination. This is especially noticeable when forms of collapse which are either permanent (thoracoplasty) or not immediately reversible (phrenicotomy) are considered. The importance, therefore, of careful selection of the procedures and of the optimum time of their application is obvious.

Table 5 shows briefly the various types of combined collapse therapy that were used in 28 selected cases for patients in whom a pleural space was absent unilaterally or bilaterally (table 1) or in whom the pneumothorax was abandoned on one or both sides (table 3). The results show that patients fare better if the measures in the combination are

TABLE 5.—*Clinical and Anatomic Results in Combined Collapse Therapy Other Than Exclusive Pneumothorax*

Form of Combination	Anatomic Result of Collapse	Working or Ambulant	Improved	Worse	Dead	Total
Pneumothorax on one side, thoracoplasty and phrenicotomy on other (alternating)	Bilateral effective	1	0	0	0	1
Pneumothorax on one side, thoracoplasty on other side (3 alternating)	Bilateral effective	2	0	0	0	2
	Unilateral effective	0	1	0	5*	6
	Bilateral ineffective	0	0	1	0	1
Pneumothorax on one side, phrenicotomy on other (in 2, alternating; in 5, phrenicotomy supplementary to bilateral pneumothorax)	Bilateral effective	4	0	0	0	4
	Unilateral effective	4	0	0	1	5
	Bilateral ineffective	0	0	0	3	3
Bilateral phrenicotomy (all alternating)	Bilateral ineffective	1	0	0	1†	2
	Unilateral effective	0	0	0	1*	1
Phrenicotomy on one side, thoracoplasty on other side (all alternating)	Bilateral effective	2	0	0	0	2
	Unilateral effective	1 ^a	0	0	1 ^a	n
Bilateral thoracoplasty	Unilateral effective	0	0	0	1	1
Totals.....		14	1	1	12	28

* Postoperative deaths.

† The patients later underwent thoracoplasty and appear in the table by the designation "n."

applied alternately. Of course, this is possible only when an effective collapse on one side is achieved by such a reversible procedure as pneumothorax or temporary phrenic interruption. This point is strikingly brought out by the figures shown in the second form of combination in the table. It will be noted that the condition of the 3 patients subjected to thoracoplasty on one side after the contralateral lung had been permitted to reexpand is improved, whereas 5 postoperative deaths occurred among the patients in whom the procedures were utilized simultaneously. While wound infection was an added factor in the causation of death in 2 cases, respiratory embarrassment played the predominant role in 3. It is for this reason that I believe that bilateral thoracoplasty, unless the lesion in the lung is truly apical, can rarely be successful. For the sake of completeness, it should be said that as time goes on the number

of cases similar to those analyzed in table 5 will be somewhat increased, but in the vast majority of the cases in the groups from which these cases were taken the prognosis is not good as long as an open lesion remains.

CONCLUSION

In conclusion, I wish to stress that of all forms of bilateral collapse therapy bilateral pneumothorax is the most effective measure. Evidence has been offered which reveals that the results with this procedure are as good as those obtained by unilateral pneumothorax and the frequency of complications is about the same with the two procedures. It is therefore felt that there should be no hesitation in giving all patients presenting cavitation in both lungs the benefit of bilateral pneumothorax. Other procedures or combinations of procedures besides bilateral pneumothorax, especially when applied simultaneously, offer good results in relatively few cases; and because of the hazards involved the selection of patients must be carefully made.

DUODENOGASTRIC INTUSSUSCEPTION

ITS CLINICAL APPLICATION AND RESULTS

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For the past five years my colleagues and I have been experimenting on dogs in an effort to determine some of the factors involved in the causation of peptic ulcer.¹ In these experiments the pyloric sphincter of the stomach was divided by a longitudinal incision down to the mucosa. Then the pars superior duodeni was invaginated into the antrum pyloricum. This procedure produced duodenogastric intussusception. The ulcer-bearing area (the pyloric end of the stomach and the first portion of the duodenum) was thereby transplanted into a new and more highly acid environment. Eight months after operation the invaginated portion remained in place and was found to be morphologically normal. In other words, a living transplant of Brunner's glands had been placed in the pyloric antrum.

Studies made with regard to acids, mucin and the emptying time led to the following conclusions:

- (a) Brunner's glands have two secretions—a local protective mucin and a systemic acid-stimulating hormone.
- (b) Hydrochloric acid stimulates the local production of mucin as well as gastrin, which in turn assures the necessary hydrochloric acid for this stimulation, thereby perpetuating the cycle.
- (c) The adventitious duodenal mucous membrane in these experiments did not show ulcer even with increased acidity and rapid emptying time. This was explained as due to the action of the defensive mechanism (mucin).

Ulcers were next produced in normal dogs by using toxic doses of cinchophen. These animals had only a slightly higher acid content but a much larger amount of mucin than normal. Since ulcers develop almost uniformly in control animals, it was thought that the amount of mucin, although increased, was insufficient to protect the mucous membrane. Ulcers could be produced in the stomach and the duodenum

From the Department of Surgery, Indiana University School of Medicine.

1. Berman, J. K., and Baxter, N. E.: Duodenogastric Intussusception: An Experimental Study of Peptic Ulcer, *Arch. Surg.* **33**:1-18 (July) 1936.

of dogs protected by duodenogastric intussusception after the administration of toxic doses of cinchophen but much less frequently and without perforation.

Our experiments proved the value of reenforcing and using the pyloric end of the stomach rather than sacrificing it, as is done in pylorotomy or gastrectomy. The operation of duodenogastric intussusception creates an artificial plica circularis (*valvula conniventes*) and delimits jetting of acid chyme. By transplanting Brunner's glands adequate mucin protection is afforded. This procedure also reenforces and immobilizes the pylorus. This is proved by the fact that peristaltic waves are not seen in this region. The ulcer is thereby permitted to heal.

We concluded that (*a*) because of its safety and ease of performance in suitable cases, duodenogastric intussusception is an aid in the surgical treatment of chronic peptic ulcer and that (*b*) if scarring of the pylorus is marked or if the ulcer is on the gastric side, excision of the ulcer with division of the pyloric sphincter followed by duodenogastric intussusception is the operation of choice.

INDICATIONS FOR SURGICAL INTERVENTION IN CASES OF ULCER

In general, patients with ulcer may be divided into three large groups: The first group includes those who respond to medical management. Although accurate statistics are difficult to evolve because so many ulcers heal undiagnosed, we feel that the great majority of patients with peptic ulcer belong in this group. The second group includes those who respond to surgical therapy. One cannot be sure of the response that will be shown by a patient to surgical treatment, but the indications for operation are clear. They may be dogmatically listed as follows: (1) perforated peptic ulcer,² (2) ulcer with obstruction, (3) ulcer with repeated hemorrhage³ (at least one repetition) and (4) chronic ulcer which will not respond to intensive medical care, especially if on the gastric side. For this group of patients almost any of the accepted surgical procedures, whether it is a pyloroplasty, gastroenterostomy or gastrectomy, if followed by good medical supervision will effect a cure.

The third group of patients may be called ulcer formers.⁴ This term may be misleading because any patient who has once had a peptic ulcer becomes an ulcer former under proper stimulation.⁴ However, here

2. Berman, J. K.: Some Consideration of Probable Exciting Factor in Perforated Peptic Ulcer, *J. Indiana M. A.* **26**:416-419 (Sept.) 1933.

3. Goldman, L.: Gross Hemorrhage from Peptic Ulcer: Its Morbidity, Mortality, and Treatment, *J. A. M. A.* **107**:1537-1542 (Nov. 7) 1936.

4. David, V.: Personal communication to the author.

it is desired to refer to the patients in whom, in spite of medical and surgical care, recurrent ulcers accompanied by complications usually develop. It is for the latter group of patients that duodenogastric intussusception seems most promising; and since, as has been stated, one cannot foretell the outcome in these cases, we feel that the most desirable operation is a conservative one which does not sacrifice tissue and which has permanent value. Such we believe is duodenogastric intussusception.

TECHNICS FOR OPERATION

Although the procedure as originally described in our previous paper¹ can be done in selected cases, we found that it is usually necessary to combine it with other forms of pyloroplasty. The original operation consisted in freeing the greater and lesser curvatures of the stomach and duodenum by dividing the hepatogastric and hepatoduodenal ligaments and the gastrocolic ligaments with the greater omentum. This is carried out from the upper portion of the antrum to a point about 1 to 1½ inches (2.5 to 4 cm.) distal to the pylorus, the extent varying with the length of the first portion of the duodenum and its mobilizability. An incision is then made down to the mucous membrane, as in the Rammstedt pyloroplasty. Then the operation is completed by pulling the stomach down over the duodenum and anchoring it with two or three tiers of interrupted silk sutures (fig. 1). However, the operation may be combined with various forms of pyloroplasty:

1. The anterior two thirds of the pylorus is resected (fig. 2).
2. If the ulcer is on the gastric side it may be excised, and the pylorus may be divided longitudinally and sewed transversely (fig. 3).
3. Or the pylorus may be divided and sewed transversely (fig. 4).
4. If the ulcer is on the posterior side and is tightly adherent to the pancreas, the pylorus may be divided, and then the ulcer may be cauterized, removed or not molested; this is followed by transverse suture and invagination of most of the circumference of the duodenum (fig. 5).
5. V resection of the ulcer on the lesser curvature is followed by division of the pylorus (fig. 6).

It is readily seen that this procedure may be used in conjunction with most types of pyloroplasty and that in addition to the lines of protecting sutures, immobilizing and reenforcing the ulcer-bearing area, it creates a living transplant of Brunner's glands supplying the protective mucin.

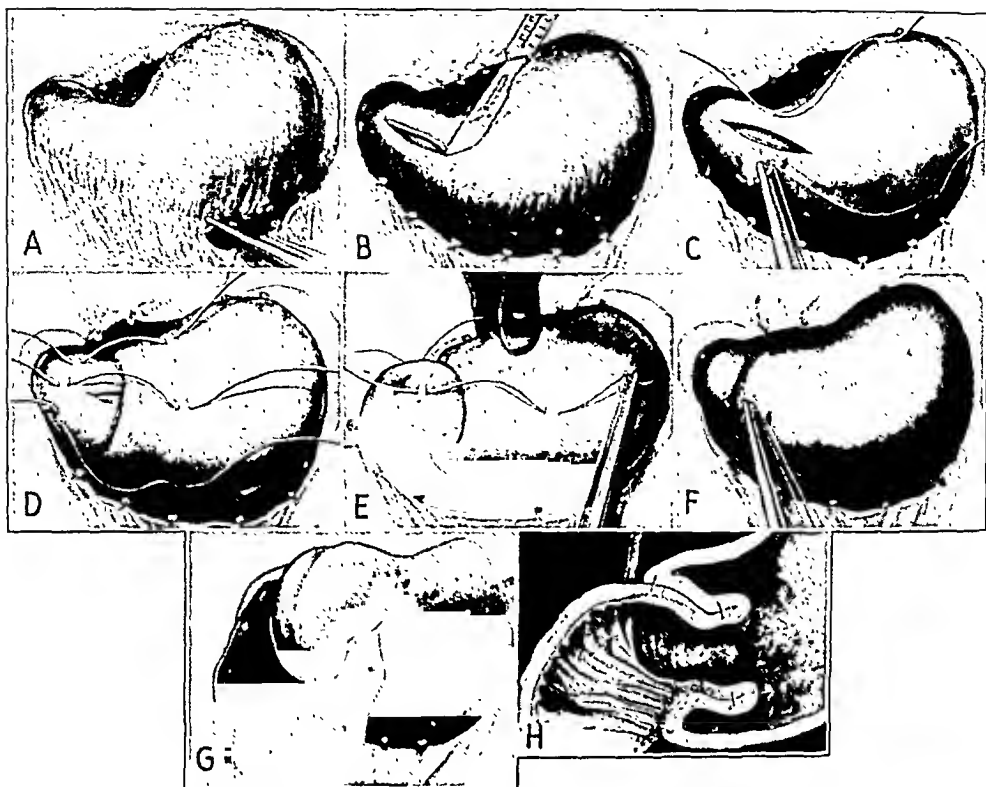


Fig 1.—Duodenogastric intussusception. *A*, division of the hepatogastric and hepatoduodenal ligaments and the gastrocolic ligament with the greater omentum; *B*, longitudinal incision of the pylorus in the manner of a Rammstedt pyloroplasty; *C*, the first tier of sutures in place so as to form a duodenogastric intussusception; *D*, the second tier of sutures; *E*, the second tier of sutures on the posterior side; *F*, extra sutures placed around the circumference to make the suture line secure; *G*, testing the patency of the pylorus with the thumb and forefinger; *H*, cross section showing the completed operation of duodenogastric intussusception.

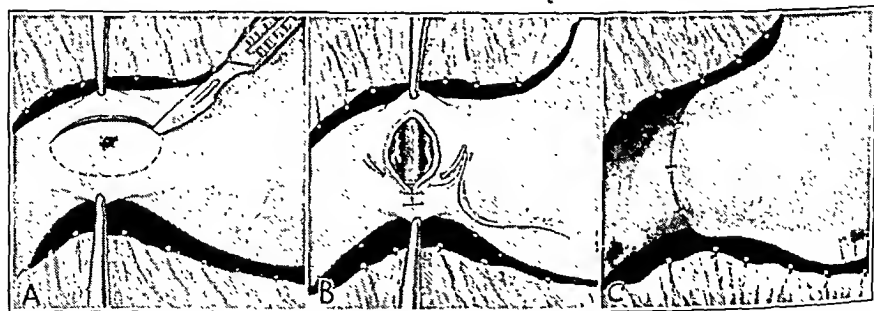


Fig. 2.—*A*, the resection of the anterior two thirds of the pylorus; *B*, transverse suture of the pylorus; *C*, duodenogastric intussusception after the pylorus has been sutured transversely.



Fig. 3.—*A*, excision of the gastric ulcer, with longitudinal incision of the pylorus; *B*, transverse suture of the pylorus; *C*, duodenogastric intussusception. The first tier of sutures is complete.

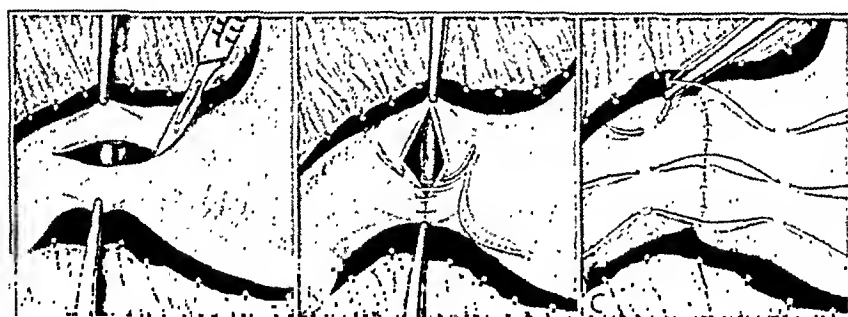


Fig. 4.—*A*, longitudinal incision of the pylorus; *B*, transverse suture; *C*, duodenogastric intussusception. The first tier of sutures is complete. The second tier of sutures is in place.

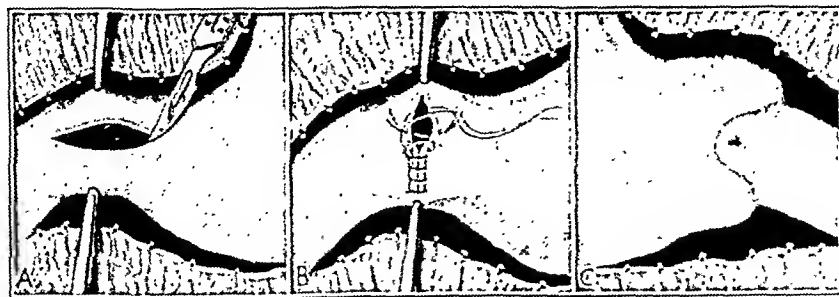


Fig. 5.—*A*, longitudinal incision of the pylorus (the ulcer is seen on the posterior side); *B*, transverse suture of the longitudinal incision; *C*, duodenogastric intussusception of approximately four fifths of the circumference (posterior view; the ulcer is adherent to the pancreas).

REVIEW OF CASES

We have carried out this operation on 5 patients thus far. The first operation was performed on Feb. 2, 1936. It will be noted that we waited six months between the first and the second and also between the second and the third operation. This was done to insure the reliability of the operation. As our technic improves, we feel that it may be used in most cases of surgical ulcer.

CASE 1.—Mr. J. M. M., aged 62, a laborer, was admitted to the Long Hospital on Feb. 2, 1936, complaining of severe abdominal pain. This had begun suddenly twenty hours before admission to the hospital. Although there was no previous history of ulcer, he stated that his stomach had been sore for three days prior



Fig. 6.—*A*, a V resection of the gastric ulcer on the lesser curvature; *B*, transverse suture of the resected area and longitudinal incision of the pylorus; *C*, duodenogastric intussusception after transverse suture of the pylorus (the first tier of sutures is in place); *D*, duodenogastric intussusception completed.

to the onset of the illness. The abdomen was extremely rigid, and there was marked tenderness in the epigastrium. The blood counts and urinalyses gave normal results. The Kline test for syphilis gave a negative reaction. Roentgenographic examination revealed pneumoperitoneum. A diagnosis of perforated peptic ulcer was made, and he was operated on within one hour after entry.

With the patient under ether anesthesia a right upper paramedian incision was made. When the peritoneum was incised, free air escaped. The duodenum was found to be markedly inflamed and covered with a thick plastic exudate. A small perforated ulcer was situated on the anterior wall of the duodenum, and a second ulcer was felt below this. The hepatogastric, hepatoduodenal and gastroduodenal ligaments were divided up to the upper portion of the pyloric antrum and down to a point about $1\frac{1}{2}$ inches (4 cm.) below the pylorus, thereby mobilizing this portion

of the stomach and duodenum. The pyloric sphincter was divided longitudinally down to the mucous membrane in the manner of a Rammstedt pyloroplasty. Then duodenogastric intussusception was done, two tiers of no. 0 chromic catgut suture being used (fig. 1)). The greater omentum was placed over the field of operation, and the abdomen was closed without drainage.

The patient made an uneventful recovery and was discharged from the hospital on February 21. On March 9 he was in good health, with no symptoms; the values for acids were within normal limits, and the value for mucin was 0.9 mg. per cubic centimeter. A barium sulfate meal was given, and the report was as follows: Preliminary fluoroscopic examination of the chest showed a heart of borderline size. The ascending aorta was slightly widened. No abnormal pulsations were visualized. The peribronchial markings were increased. There was good excursion of the diaphragm. Studies of the gastrointestinal tract showed normal fillings of a J type of stomach. Rugae were regular throughout. The distal end of the pylorus and the bulb were deformed, probably owing to the previous operative procedure. A portion of the duodenal bulb had been invaginated into the distal portion of the pylorus, leaving only the terminal end of the first

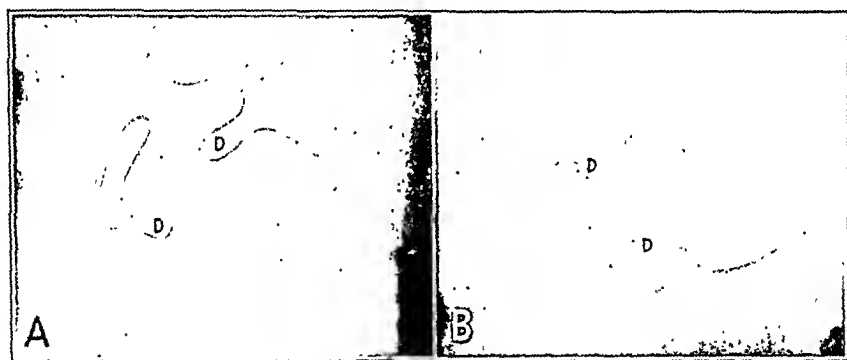


Fig. 7 (case 1).—*A*, roentgenogram (retouched) showing the duodenum invaginated into the pyloric antrum (immediately after operation); *B*, six months later, showing the permanency of the duodenogastric intussusception. Note the widened pylorus. *D* indicates duodenum.

portion of the duodenum well visualized. This was flattened and broadened, and the distal end of the pylorus, which had been brought down, was considerably wider than normal. The second portion of the duodenum was well visualized. The operative procedure apparently caused mild deformity in the greater curvature of the distal end of the pylorus. At six hours the stomach was empty, and the head of the meal was in the transverse colon. The patient was given a second barium meal in order to permit the rechecking of the findings (fig. 7 *A*).

On September 9 he was asked to return, and another barium meal was given, the report being as follows: There was considerable improvement in the condition of the distal end of the pylorus and the bulb. At six hours the stomach was empty, and the head of the meal was in the transverse colon. The pyloroplasty was apparently functioning well (fig. 7 *B*).

The patient has remained free from symptoms.

CASE 2.—Mr. A. U., aged 55, an unemployed laborer, was admitted to the Long Hospital on June 16, 1936, with complaints of loss of weight, insomnia, and pain and discomfort in the abdomen. His past history revealed that he had had pain

in the abdomen since 1924. A medical regimen for two years failed to relieve his symptoms. On March 2, he was operated on. The surgeon said he felt that the lesion was an inoperable carcinoma, and after taking a lymph gland for biopsy he closed the abdomen without further surgical intervention. The lymph gland proved to be an inflammatory enlargement. The patient improved somewhat after this procedure but was readmitted to the Long Hospital on June 16 with recurrence of the symptoms.

Physical examination showed that he had lost a great amount of weight and that he had a palpable thyroid gland and extreme tenderness in the epigastrium.

Laboratory examination showed: urine, normal; phenolsulfonphthalein test, 70 per cent for two hours; red blood cells, 4,170,000; hemoglobin, 12 to 13 Gm.; white blood cells, 6,200 to 13,250; serologic tests, negative reaction; stools, 1 plus to 4 plus blood; basal metabolic rate, —1 per cent. An alcohol and histamine test⁵ showed high acidity, up to 73 per cent free hydrochloric acid, total acid,

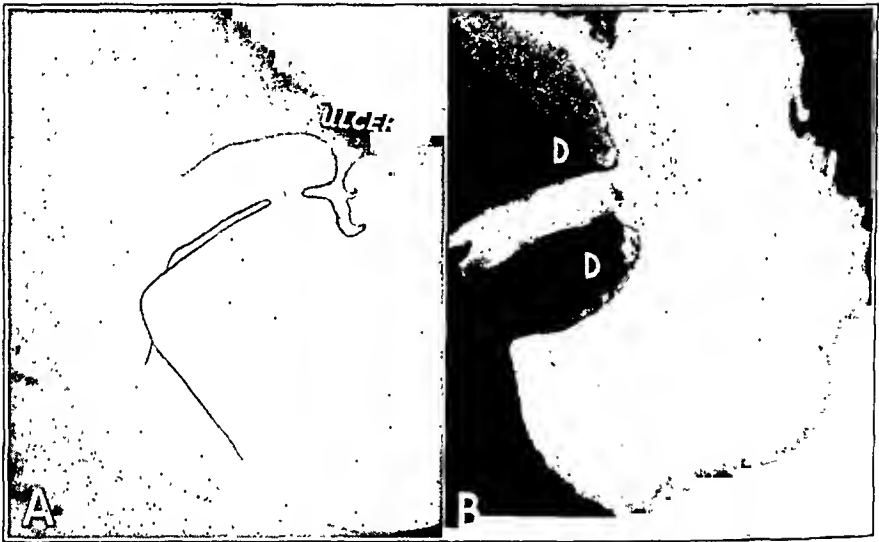


Fig. 8 (case 2).—*A*, roentgenogram (retouched) taken before operation, showing the peptic ulcer on the lesser curvature and the defects of the bulb; *B*, seventeen days after operation, at which the ulcer was removed and the duodenum invaginated.

79 per cent, and lactic acid, 0. Blood was present in all specimens. The p_n was 5.5. No determination of mucin was made prior to operation. The roentgenographic examination showed a large penetrating ulcer on the lesser curvature, with complete retention at the end of six hours (fig 8*A*). He was placed on Sippy management but made no progress, as determined clinically, by roentgenographic study and by gastric analyses.

5. Alcohol and histamine tests are performed in the Long Hospital as follows: After the stomach is emptied, the patient is given 200 cc. of 7 per cent alcohol. Then 0.5 mg. of histamine is given subcutaneously (0.2 mg. is given if the patient is a woman). The stomach contents are then aspirated every fifteen minutes for one hour. The average normal value agrees with that reported by Lerman and his associates (Lerman, J.; Pierce, F. D., and Brogan, A. J.: Gastric Acidity in Normal Individuals, *J. Clin. Investigation* 11:155-165 [Jan.] 1932): about 41 per cent free hydrochloric acid and about 51 per cent total acid.

the outpatient department three months later, at which time he made a vague complaint of general pains over the entire body. On March 1, 1937, a letter written to the patient brought no reply; however, his family physician reported him to be in good health. On June 4 another letter was written to him inviting him to return to the outpatient department if he still had any symptoms. He did not respond to this, although he lived but a short distance from Indianapolis. We assumed, therefore, that he was in a good state of health at that time.

Summary.—This patient with recurrent chronic gastric ulcer had had three years of medical management and a previous operation for ulcer. After the operation herein described he was clinically improved, and the acid values returned to normal. Although the roentgenogram showed some retention immediately after the operation, this condition evidently did not persist because no symptoms of retention appeared. The pylorus had probably been opened by the lateral pull of the wall of the stomach. As far as is known now, the patient remains clinically well.

CASE 3.—Mr. H. W., aged 37, a laborer, was admitted to the Long Hospital on May 8, 1937. His chief complaint was of pain in the epigastrium, which was not relieved by careful diet and alkaline powders.

Sixteen years before his admission to the hospital appendectomy was performed elsewhere. For the past six years he had had pain in the epigastrium coming on about two hours after meals. This was relieved by food.

The patient was a thin man with a scar in the right lower quadrant of the abdomen. There was tenderness in the epigastrium with muscle spasm. In the medical department a careful study was made, and it was found that he had pyelitis and cystitis and that the urine was loaded with pus and red blood cells. However, repeated cystoscopic examination revealed no stones. The white blood cell count varied from 6,400 to 14,750. Roentgenographic examinations were repeatedly made, and an opaque shadow was always seen in the right upper quadrant. This proved later to be caused by the gallbladder, which was filled with stones. Tetraiodophenolphthalein sodium was injected, but the gallbladder was not visualized. Barium meal revealed normal filling of a rather large stomach. There was a large niche showing retention on the posterior wall of the lesser curvature of the fundus of the stomach which was probably due to ulcer (fig. 9A). Slight tenderness was noted over this area. At twenty-four hours there was normal movement of the meal. Gastric analyses made prior to operation showed: free hydrochloric acid, 80; total acid, 86 (average); blood, 0; mucin, 0; p_n of gastric contents, 4. The stools repeatedly showed blood. The phenolsulfonphthalein test showed: first fifteen minutes, a 17.5 per cent output, and first half hour, a 32.5 per cent output.

On April 13 operation was performed, and the following note was made: With the patient under ether anesthesia the abdomen was entered through a right upper paramedian incision. Exploration of the abdomen revealed a duodenal ulcer on the lesser curvature just below the pylorus. The gallbladder was markedly distended and was found to contain one stone.⁶ The right kidney was slightly

6. Three of these patients had gallstones. In 1932 we presented a paper before the Indiana University Post-Graduate Course on the incidence of gallstones and peptic ulcer. We found this association to be present in about 5 per cent of cases. Whereas cholelithiasis may be accompanied by a low or high gastric acid content (this explains relief with sodium bicarbonate in some and dilute hydrochloric acid in others), in the patients with ulcer the values for acids were uniformly high. These patients were to have operations on the gallbladder later.

arged and was relatively low but not movable. The pyloric antrum, the pylorus and the first portion of the duodenum were mobilized by division of the hepatoduodenal, hepatoduodenal and gastrocolic omentum between ligatures. The ulcer was sutured together with a portion of the pylorus, which was then sutured transversely with no. 0 chromic catgut sutures, thereby widening the pyloric canal. The stomach was brought down over the duodenum, in the manner of a duodenogastrostomy, by two tiers of interrupted silk suture. The omentum was brought over the field of operation, and the abdomen was closed without drainage, with no. 0 chromic catgut sutures in the fascial and interrupted silk sutures in the skin (fig. 2).

On April 19 (fifth postoperative day) an alcohol and histamine meal was given with the following results: free hydrochloric acid, 51, and total acid, 66; the mucin content was not determined. However, this test was repeated on April 30, and the results showed a maximum free hydrochloric acid content after alcohol and histamine meal of 51 and a hydrochloric acid content during fasting of 10. There was no blood, and the total acid content was 66. The value for mucin was 72 mg. per hundred cubic centimeters. The pathologic report

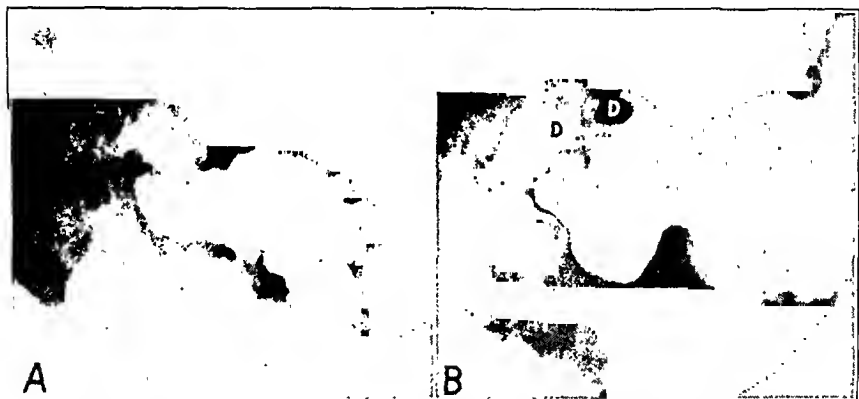


Fig. 9 (case 3).—*A*, roentgenogram (retouched) taken before operation, showing defects of the bulb; *B*, sixteen days after operation, showing the duodenogastrostomy. Note the peristaltic wave. This does not follow through the invaginated portion but is carried on into the duodenum.

the tissue removed at operation was as follows: duodenal ulcer, with no indication of malignancy; one lymph node showed nonspecific hyperplastic changes. Roentgen examination of the gastrointestinal tract on April 30 showed normal emptying of the stomach. There was marked deformity of the distal end of the pylorus and the bulb (apparently from the operative procedure of duodenogastrostomy). There was good emptying of the stomach. Slight dilatation of the second and third portions of the duodenum was noted. At six hours there was a slight trace of barium in the stomach, and the head of the meal was in the transverse colon. At twenty-four hours there was a normal movement of the meal (fig. 9*B*).

This patient was discharged from the hospital on May 1 in an excellent state of health and completely relieved of his symptoms.

He was admitted on May 8 for a check-up. He was entirely free from symptoms, and gastric analysis showed during fasting free hydrochloric acid of 0 and total acid of 10; after the alcohol and histamine meal the total acid was 66 and free hydrochloric acid of 51.

Summary.—This patient had a chronic gastric ulcer with complicating cholecystitis and cholelithiasis, pyelitis and cystitis. Medical management over a long period failed to relieve his symptoms. After the operation as herein described the patient was relieved of all gastric symptoms, the values for acids returned to normal limits⁷ and the follow-up study showed him to be clinically well.

CASE 4.—Mrs. N. W., aged 52, a widow, was admitted to the Long Hospital on May 22, 1937. She complained of vomiting for the past four weeks, loss of weight (26 pounds [11.8 Kg.]) and arthritis. She had been operated on elsewhere seven months previously for a perforated ulcer, with satisfactory recovery; but she vomited just before discharge from the hospital and since that time had vomited occasionally. She had vomited every day for the past three weeks. Arthritis had been present for the past four years.

Physical examination showed a scar over the upper portion of the right rectus muscle, beneath which was a firm mass. There was no tenderness or rigidity; the abdomen was scaphoid.

The blood pressure on entry was 105 systolic and 70 diastolic. The red blood cell count was 4,610,000 and the white blood cell count 7,500. The stool contained 3 plus blood on May 31. Urinalyses showed specimens ranging from those with 6 plus cells to those loaded with pus.

Analysis of the stomach contents on May 27 showed 3 plus blood, and a p_H of 6. Gastric analysis on June 2 showed a total acid of 30, free hydrochloric acid of 10 and 94 mg. of mucin per hundred cubic centimeters.

Roentgen examination of the gastrointestinal tract after ingestion of a barium meal on May 24 showed normal filling of a large ptotic stomach. Peristalsis was exceedingly vigorous. Considerable time elapsed before the barium passed beyond the pyloric end of the stomach. The bulb was small but did not appear to be greatly deformed. The second and third portions of the duodenum were well visualized. There did not appear to be any abnormality in this area. However, there was about 70 per cent retention at five hours. At twenty-four hours there was normal progress of the meal, with 15 per cent retention in the stomach. The diagnosis was partial obstruction, possibly due to ulcer, although none was visualized (fig. 10 A).

An operation was performed on June 4. With the patient under ether anesthesia the abdomen was opened through a right paramedian incision mesial to the scar of the previous operation. The stomach and duodenum were densely adherent to the parietal peritoneum so that careful dissection had to be made to reach the pylorus. Exploration revealed a thickened gallbladder filled with small calculi. The pancreas was found to be normal. The common duct was not enlarged and apparently was without obstruction. The duodenum had one large diverticulum on its superior margin just distal to the pylorus. The pylorus was thickened and narrowed down to the size of a lead pencil. The scar of the previous ulcer was found; it was on the gastric side and was not active. After the pyloric antrum and pars superior duodeni had been carefully freed, all bleeding areas were tied doubly with transfixing ligatures on both sides. The pylorus was then incised longitudinally, and careful inspection was made of the duodenum, which showed the diverticulum previously referred to. The ampulla of Vater could be seen after the incision had been prolonged, and bile was found to be freely spurting into the duodenum. The mucosa was pale. The lumen of the stomach was explored and was found to be without new growth or active ulcer. The rugae were small and

7. This coincides with the findings in our experimental work. The values for acids remain about normal, but the amount of mucin is increased.

seemed to be absent in places. The mucous membrane was pale and smooth, but in spots small hemorrhagic areas were seen. The longitudinal incision was sutured transversely with no. 0 plain catgut. This was turned in by means of interrupted silk sutures placed entirely around its circumference. Two tiers of these sutures were used, forming a duodenogastric intussusception. The omentum was brought down over the field of operation, and the abdomen was closed in layers without drainage with a no. 0 plain catgut continuous suture for peritoneum, no. 0 plain interrupted sutures on the rectus muscle and no. 1 chromic catgut cross stitch interrupted sutures on fascia. A black silk mattress on edge suture was used for the skin (fig. 4).

The postoperative course was uncomplicated.

Gastric analysis on June 19 (fifteenth postoperative day) showed free hydrochloric acid of 0, total acid of 20, no lactic acid, no blood and no significant

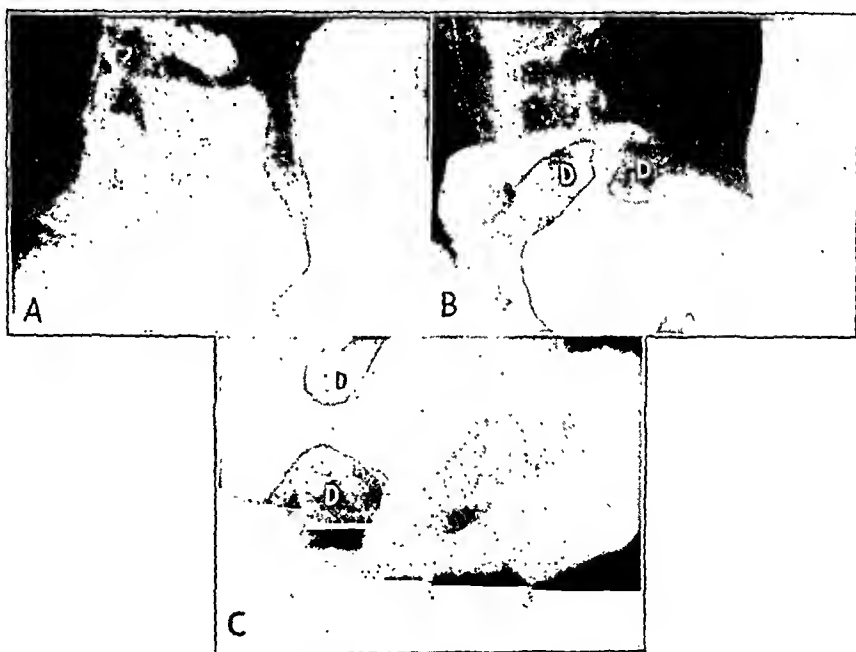


Fig. 10 (case 4).—*A*, roentgenogram taken before operation, showing the J type of ptotic stomach and the almost completely obstructed pylorus; *B*, seventeenth day after operation (note the improved position of the stomach and the invaginated duodenum); *C*, closer view of the duodenogastric intussusception.

organism. Alcohol and histamine gastric analysis on June 26 showed: free hydrochloric acid, 0; total acid, 14; lactic acid, 0; blood, a trace; p_{H} 4, and mucin, 89 mg. per hundred cubic centimeter. Gastric analysis (alcohol and histamine) on June 30 showed: free hydrochloric acid, 32; total acid, 38; lactic acid, 0; blood; p_{H} , 8, and mucin, 89 mg. per hundred cubic centimeters.

Postoperative roentgen examination of the gastrointestinal tract after the ingestion of a barium meal showed good filling of a rather large stomach; narrowing of the distal end of the pylorus; considerable irritability over this area; persistent deformity of the duodenum, pylorus and bulb, which is found in duodenogastric intussusception (operative procedure), and mild dilatation of the second and

third portions of the duodenum. At six hours there was a trace of barium in the stomach, and the head of the meal was progressing normally. At twenty-four hours the colon was nearly empty.

The patient was discharged from the hospital on June 30 free from all gastrointestinal symptoms.

CASE 5.—Mrs. C. E., a housewife, aged 41, was admitted to the Long Hospital on June 22, 1937. She complained of pain in the epigastrium, left shoulder, neck and face; loss of weight (70 pounds [31.8 Kg.] in two and one-half years), and nausea and vomiting. She had had pain in the left shoulder and in the left side of the neck for eight to ten years. There had been some gastric discomfort during this time, and she complained of extreme nervousness.

Physical findings included evidence of loss of weight, an edematous throat, a lipoma at the insertion of the left deltoid, no masses or tenderness in the abdomen, hyperactive reflexes and retroversion of the uterus. The blood pressure on entry was 150 systolic and 100 diastolic, the temperature 98.6 F. and the pulse 90.

Laboratory examination showed: hemoglobin, 10 Gm.; red blood cells, 3,220,000 to 3,400,000, and white blood cells 7,500 to 8,050. Urinalyses showed: albumin, slight trace, and pus cells, occasional to 20. The phenolsulfonphthalein test showed an output which varied from 5 to 15 per cent for fifteen minutes. On entry gastric analyses showed: free hydrochloric acid, 74; total acid, 109, and blood, plus. The patient was placed on the Sippy management. Gastric analyses showed: on June 25, free hydrochloric acid, 59; total acid, 78, and blood, plus; on June 26, free hydrochloric acid, 54; total acid, 88, and blood, plus; on June 27, free hydrochloric acid, 10; total acid, 79, and blood plus; on June 28, free hydrochloric acid, 49; total acid, 56 and blood, 0. Alcohol and histamine gastric analysis on July 3 showed: free hydrochloric acid, 0; total acid, 14; lactic acid, 52; blood, 0, and mucin, 0. The Mosenthal test showed a variation in the specific gravity from 1.008 to 1.01. The total nonprotein nitrogen content of the blood on June 28 was 42 mg. On July 3 the nonprotein nitrogen content of the blood was 55 mg. per hundred cubic centimeters, the urea nitrogen content was 28 mg. and the creatinine content was 1.8 mg.

Preliminary fluoroscopic and roentgenographic examination of the chest showed mild bronchial increase of the pulmonary fields, with some small calcifications. There was good excursion of the diaphragm. Studies of the gastrointestinal tract (the patient was given part of a meal) showed a markedly enlarged ptotic stomach. Some fluid was present before ingestion of the barium. At no time were we able to visualize the bulb. At six hours there was about 80 per cent retention in the stomach. Otherwise there was normal progress of the meal. The diagnosis was stenosing ulcer (fig. 11A).

On July 6 the patient was operated on under ether anesthesia. The abdomen was opened through an upper right paramedian incision. Exploration of the abdomen revealed a large liver, extending about 2 inches (5 cm.) below the costal margin; the gallbladder was enlarged and filled with stones; the duodenum had a large ulcer on the posterior side which was adherent to the pancreas; the pancreas was found to contain a small cyst, about the size of a walnut. The hepatogastric and hepatoduodenal ligaments were carefully divided between catgut ligatures, and the posterior portion of the stomach was explored. A large ulcer was found distal to the pylorus and adherent to the pancreas. The gastrocolic ligament and the greater omentum were divided from a point corresponding to the superior edge of the pyloric antrum to a point about $1\frac{1}{2}$ inches (4 cm.) distal to the pyloric sphincter. The pylorus was found to be obstructed. It was divided longitudinally, and the ulcer was clearly seen on the posterior wall of the duodenum.

It was about the size of a 10 cent piece. The longitudinal incision was closed transversely with a continuous lockstitch of no. 0 chromic catgut. The stomach was brought down over the suture line with interrupted silk sutures in two tiers, producing duodenogastric intussusception. The patency of the pyloric sphincter was tested and found to be normal. The greater omentum was sutured down over the field of operation, and the abdomen was closed without drainage

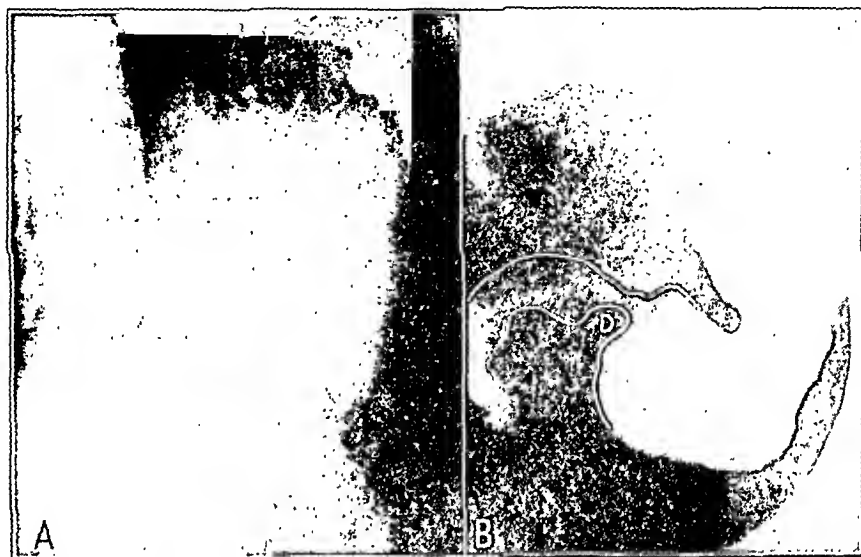


Fig. 11 (case 5).—*A*, roentgenogram (lateral view) taken before operation (note the deformed pylorus); *B*, roentgenogram (retouched) taken two weeks after operation, showing the duodenogastric intussusception after longitudinal division and transverse suture of the pylorus.

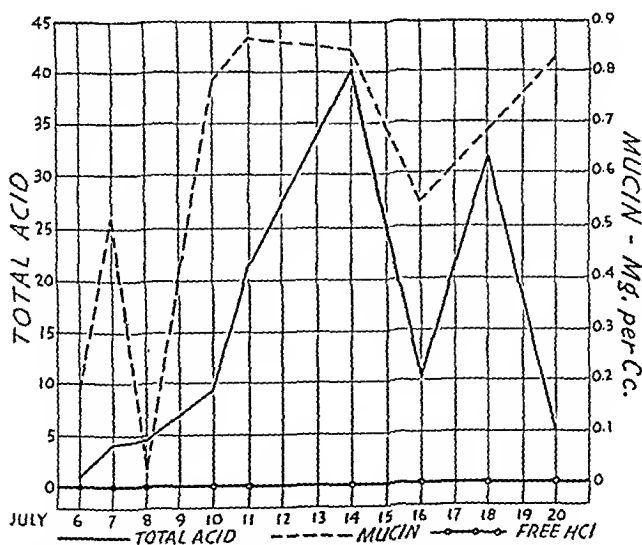


Fig. 12 (case 5).—Chart showing the curves obtained for gastric acids and mucin after operation without the ingestion of an alcohol and histamine meal.

with no. 0 plain catgut on peritoneum and muscle, no. 0 chromic catgut on fascia and interrupted silk sutures on skin (fig. 5).

Postoperative gastric analyses in this case revealed uniform absence of free hydrochloric acid, with a variable total acid content and a high mucin content (fig. 12).

The patient made an uneventful recovery, and on August 20 she was given a barium meal, and some degree of obstruction was still evident at the pylorus. On August 21 (forty-seven days after operation) an alcohol and histamine meal revealed (fourth specimen): total acid, 68; free hydrochloric acid, 60, and mucin, 23.

This case illustrates the feasibility of the operation in cases of posterior adherent ulcer. However, it is suggested that every effort be made to free the ulcer so that the complete operation can be performed. This was the only case in which there was evidence of persistent partial obstruction after one month and the only one in which there was a high acid content after the ingestion of an alcohol and histamine meal, although the mucin value also was high. The patient is now free from symptoms.

SUMMARY OF RESULTS

The operation was entirely satisfactory in all but the last case. There were no deaths, and a follow-up study showed the patients to be clinically well. The acid values remained within normal limits or low and the mucin content high. (According to Anderson and Fogelson,⁸ the normal average is 0.4 to 0.7 mg. per cubic centimeter. Our patients showed values up to 2.2 mg.) Roentgenograms made post-operatively showed the invaginated duodenum as a large fold pointing into the lumen of the pyloric antrum. At first it was thought that this might narrow the lumen and cause partial pyloric obstruction in those patients without longitudinal division and transverse suture of the pylorus. However, our follow-up roentgenograms clearly demonstrated that the lateral pull of the stomach opens the pylorus wider than normal. In case 5 the narrowing persisted longer than in the others. In the woman with marked gastropotosis the stomach assumed a more normal position.

CONCLUSIONS

From the small group of cases studied we may conclude that the operation which we have called duodenogastric intussusception should have a place in the surgical attack on peptic ulcer.

The comparative ease of performance, low mortality rate and excellent clinical results seem to indicate that this procedure is rational and practicable.

8. Anderson, R. K., and Fogelson, S. J.: The Secretion of Gastric Mucin in Man: A Comparative Study in the Normal Subject and in the Patient with Peptic Ulcer in Response to an Alcohol Test Meal, *J. Clin. Investigation* 15:169-172 (March) 1936.

ORIGIN OF CARCINOMA IN CHRONIC GASTRIC ULCER

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Almost a century ago, Cruveilhier¹ distinguished between peptic ulcer and carcinoma of the stomach and expressed the opinion that in certain cases malignant degeneration of a peptic ulcer might occur. Since then a voluminous literature, more or less controversial, has accumulated on the question of malignant degeneration of a preexisting benign ulcer of the stomach. It is now generally conceded that so-called "ulcer-carcinoma"² does exist as a pathologic entity. The point about which discussion still centers, however, is the incidence of such a lesion.

Cabot and Adie³ reviewed 82 reports in the literature and noted that approximately half the authors concluded that the development of carcinoma from ulcer occurs in less than 10 per cent of cases.

Newcomb,⁴ in a comprehensive survey, listed the statistics of 102 observers who estimated the proportion of gastric carcinomas originating in primary benign ulcers. Among these, 51 stated that not more than 10 per cent of gastric carcinomas arise in peptic ulcer, 74 announced the incidence to be less than 20 per cent and 15 recorded figures exceeding 50 per cent. The entire series covered a range from zero to "over 90 per cent."

Hauser⁵ assembled the statistics based on pathologic anatomic studies of a large series of gastric ulcers from several German clinics. He found that only 3.4 per cent of a collected group of 1,774 gastric ulcers showed evidence of carcinomatous change and that the average incidence in the individual reports was 2 per cent. His figures are shown in table

From the Laboratories and Surgical Services of the Mount Sinai Hospital.

1. Cruveilhier, J.: *Anatomie pathologique du corps humain*, Paris, J. B. Baillière, 1829-1835, vol. 1; 1835-1842, vol. 2.

2. In this paper the term "ulcer-carcinoma" will be used to designate a carcinoma which has developed in a primary benign chronic gastric ulcer.

3. Cabot, H., and Adie, G. C.: *Etiology of Cancer of the Stomach*, Ann. Surg. 82:86, 1925.

4. Newcomb, W. D.: *The Relationship Between Peptic Ulceration and Gastric Carcinoma*, Brit. J. Surg. 20:279, 1932.

5. Hauser, G.: *Die krebsige Entartung des chronischen Magen- und Duodenalgeschwürs*, in Henke, F., and Lubarsch, O.: *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1926, vol. 4, pt. 1, pp. 497-518.

1, reproduced from his monograph. Two of the most recent papers on the subject, however, reported figures which are at variance. Gömöri⁶ found 6 tumors which he designated as ulcer-carcinoma in a group of 64 chronic gastric ulcers and 26 carcinomas. He concluded that "because carcinoma relatively frequently arises in peptic ulcer, such ulcers should be resected whenever possible." Newcomb,⁴ on the other hand, found only 6 ulcer-carcinomas in a series of 160 chronic gastric ulcers and 46 carcinomas.

It is obvious that the wide variation in the frequency of ulcer-carcinoma as reported in the literature depends on the type of cases selected for study and on the methods employed. Necropsy material is generally unsuitable because by the time a patient has died as the result of his gastric cancer the lesion has usually progressed to such an

TABLE 1 (From Hauser's Monograph).—Frequency of Ulcer-Carcinoma Based on Pathologic-Anatomic Statistics

Author	Clinic	Number of Ulcers	Number of Ulcer-Carci- nomas	Per Cent
Seheuermann.....	Munich.....	96	1	1.0
Berthold.....	Berlin.....	294	4	1.3
Wolowelsky.....	Basel.....	189	2	1.4
Cohn.....	Kiel.....	295	6	2.0
Grells.....	Kiel.....	186	4	2.9
Schnelder.....	Munich.....	89	3	3.4
Brinkmann.....	Kiel.....	725	40	5.5
Total.....		1,774	60	3.4
				Average 2%

extent that any possible preexisting ulcer has been completely overgrown by the malignant growth. In 4,400 autopsies done at this hospital, only 1 tumor suggestive of ulcer-carcinoma was found, and the patient with this tumor had died of a cause unrelated to the gastric lesion.

The percentage, of course, varies according to whether the incidence of the condition is sought in a series of ulcers or in a series of carcinomas.

The incidence of ulcer-carcinoma also depends on the type of patients treated in a particular clinic and on the methods of treatment used by that clinic. That is to say, if patients with gastric disturbances apply for treatment early in the course of the disease a larger number of operable carcinomas will be found; this will provide a larger number of specimens for study. Should the method of treating patients with peptic lesions be radical, a larger series of ulcers will also become available. Conversely, if most of the ulcers are treated medically the statistics

6. Gömöri, G.: Carcinoma Arising from Chronic Gastric Ulcer, *Surg., Gynec. & Obst.* 57:439, 1933.

obtained from observation of the relatively small number of operative specimens will not provide a true index of the incidence of ulcer-carcinoma.

The wide variations in the reported statistics are probably due to the lack of definite criteria on which to base the diagnosis of ulcer-carcinoma. Newcomb⁴ noted in his review of the literature that some of the figures were based on clinical examinations, some on roentgenologic evidence, some on histories and comparatively few on precise anatomic studies. It is on the last-mentioned class that one must depend for the diagnosis of ulcer-carcinoma. Clinical evidence, although frequently suggestive, is too often misleading.

The history presented by the patient is often unreliable. Experience indicates that symptoms of other conditions may clinically simulate the typical symptoms of peptic ulcer. Among these conditions are the psychoneuroses, simple functional disturbances, gastritis, duodenitis, cholecystitis and cholelithiasis. Further, one often sees patients with primary carcinoma of the stomach whose symptoms definitely suggest the presence of peptic ulcers. Maes and McFetridge⁷ studied 200 surgical cases of gastric cancer and noted that 50 of the patients had presented histories perfectly typical of ulcer.

Even a prolonged history of symptoms may not be of value in the diagnosis. Hauser⁵ stated that the scirrhus form of gastric cancer may produce an illness of several years' duration and quoted Leberts' statistics on 103 cases, in 9 per cent of which the cancer had a duration up to two years and in 8 per cent a duration up to four years.

It is not unusual to find free hydrochloric acid persisting in the gastric contents of patients with undoubted primary gastric carcinoma; even hyperchlorhydria is occasionally noted.

With the aid of roentgen examination it is possible to make an accurate diagnosis of gastrointestinal lesions in a large number of cases. Nevertheless, there is no picture characteristic of ulcer-carcinoma, and not infrequently it is impossible to state from a given examination whether the gastric ulcer is benign or malignant.

Finally, evidence obtained at a previous operation, such as exploratory laparotomy, suture of a perforated gastric lesion or gastroenterostomy, cannot be relied on. Every surgeon is familiar with the difficulty in differentiating between benign ulcer and carcinoma by examination of the lesion in situ. In addition, there are lesions which are difficult to diagnose even when the stomach is opened; microscopic study of such

7. Maes, U., and McFetridge, E. M.: *The Place of Surgery in the Therapy of Peptic Ulcer*, New York State J. Med. 36:1399 (Oct. 1) 1936.

lesions is required to determine their nature. Anschütz and Konjetzny⁸ found, on the basis of extensive statistics, that in only 3.3 to 6.9 per cent of cases in which gastroenterostomy was performed for ulcer did carcinoma appear later. In 2.5 to 4.9 per cent of these cases, the carcinomas occurred within two years; in only 1.1 to 3.4 per cent did it occur after a longer interval. Only in the latter group could the lesion be assumed to be carcinoma ex ulcere.

Hauser,⁵ in commenting on these findings, suggested that if the carcinoma occurred within two years after the gastroenterostomy it might have been present at the time of the operation.

ANATOMIC CONSIDERATIONS

The anatomic diagnosis of ulcer-carcinoma involves two problems: first, to establish proof of the preexistence of a benign chronic peptic ulcer and, second, to demonstrate the presence of malignant degeneration.

DIAGNOSIS OF CHRONIC GASTRIC ULCER

Gross Features.—Chronic callous gastric ulcer, as a rule, occurs singly and is generally situated along or close to the lesser curvature in the antral portion of the stomach. It may occasionally be found near the cardia or in the body of the stomach, but this is uncommon. The defect may be round, oval or eccentric in shape, with its long axis either parallel with the lesser curvature or horizontal so that it saddles it. The margins are usually smooth, and the surrounding mucous membrane is injected and inflamed in varying degree, yet is freely movable on the submucosa. While the edges may have a sharply punched out appearance, it is more common to find the superior edge overhanging and steep while the distal border slopes upward gradually in steplike or terrace formation, so that a longitudinal cross section through the center of the lesion resembles a fish hook or an inverted funnel. Hauser⁵ concluded that this characteristic shape of the ulcer is dependent on the normal vascular distribution in the gastric wall. This opinion is opposed to the mechanical theory supported by Rothman,⁹ Stromeyer,¹⁰ and others who have contended that the chronic gastric ulcer retains its characteristic form mainly through the mechanical effect

8. Anschütz, W., and Konjetzny, G. E.: *Die Geschwülste des Magens*, in Billroth, T., and Luecke, A.: *Deutsche Chirurgie*, Stuttgart, Ferdinand Enke, 1921, vol. 46, pt. 1, pp. 72-102.

9. Rothman, A.: *Chronisches Magengeschwür in seiner Beziehung zum Magenkrebs*, Arch. f. klin. Chir. **175**:201, 1933.

10. Stromeyer, F.: *Die Pathogenese des Ulcus ventriculi, zugleich ein Beitrag zur Frage nach den Beziehungen zwischen Ulcus und Carcinom*, Beitr. z. path. Anat. u. z. allg. Path. **54**:1, 1912.

of the passage of the gastric contents along the *magenstrasse*. The depth of the crater varies considerably in different specimens, depending on the phase in which the ulcer is seen, that is, the degree of destruction relative to the amount of healing that has taken place. The surface of the base of the ulcer may be covered with mucus, fibrin, necrotic debris or mucopurulent exudate. Considerable inflammation is frequently evident on the serosal surface in the region of the ulcer with the production of adhesions to surrounding structures, such as the transverse mesocolon, the liver and, more particularly, the pancreas. Occasionally, penetration has advanced to such a degree that the entire thickness of the base of the ulcer is destroyed and the floor of the ulcer consists actually of the agglutinated surface of the liver or the pancreas.

Occasionally, however, a chronic peptic ulcer may present an atypical gross appearance because of the severe distortion produced by cicatrization and adhesions. This may also occur after a previous surgical operation on the stomach, such as suture of a free perforation.

Histologic Features.—The microscopic examination of the chronic gastric ulcer necessarily includes a consideration of both its base and its margins. Even more than the gross picture, the microscopic picture of the structure of the peptic ulcer depends on the phase of destruction and repair present at the time of examination. In the active stage, the bed of the ulcer presents several fairly well defined zones (Askanazy¹¹): (1) a film of mucus on the surface; (2) a fibrinopurulent layer; (3) a layer of necrotic debris enmeshed by fibrin; (4) a zone of granulation tissue; (5) a stratum of dense fibrous tissue showing the evidences of chronic inflammation (in some cases there is considerable vascularization; in others blood vessels may be scarce), and (6) the serosal layer.

When the process of repair predominates, the base of the ulcer consists essentially of a mass of scar tissue on the surface of which is a narrow layer of necrotic material and fibrinopurulent mucus. If there has been severe destruction of the gastric wall the floor may be extremely thin, and occasionally one finds pancreatic or hepatic tissue in the base of the defect.

Most important is the fact, described by Hauser⁵ and accepted by most authors, that the base of the ulcer is almost always entirely free of muscularis. The segment of the muscularis corresponding to the area of the ulcer is completely destroyed, and the free ends of the muscular layer characteristically bend upward into the ulcer margin, sharply demarcated against the connective tissue of the base. This is in contrast to the condition, seen in many carcinomas, in which there is retention of the muscularis in the base with splitting and separation

11. Askanazy, M.: L'étiologie et la pathogénie de l'ulcère rond de l'estomac, Rev. méd. de la Suisse Rom. 40:477, 1920.

of the muscle fibers by the infiltrating malignant cells. Frequently, this turning up of the muscularis into the ulcer margins can be seen in cross sections with the naked eye.

Newcomb⁴ described an additional feature which he considered pathognomonic of benign chronic gastric ulcer. This consists of the close approximation or fusion of the muscularis propria and the muscularis mucosae at the edge of the ulcer, produced by the contraction of scar tissue in the process of healing. He found this condition in some part of all but 1.5 per cent of 154 chronic gastric ulcers. Gömöri,⁶ however, reviewed 64 cases of chronic ulcer of the stomach and found actual fusion of the two muscular layers in but 34 cases. There was some approximation in 22 cases, and the position was unchanged in 5 cases. In 3 instances distinct progressive separation of both layers toward the edge of the ulcer was observed. He stated that whether or not the sign described by Newcomb⁴ is found depends largely on the phase of destruction or healing which happens to prevail at the time of the examination.

The blood vessels in the floor of the ulcer frequently show endarteritis and thrombophlebitis. All stages of involvement may be encountered, including thrombosis, organization and recanalization. Occasionally a fortunate section shows a vessel near the surface undergoing destruction, thus demonstrating the mechanism of hemorrhage.

The reparative process on the part of the mucous membrane at the edge of the ulcer often produces bizarre epithelial overgrowths. These may occur as small clumps of cells, as narrow cords or as abnormal acini made up of cells which may exhibit varying degrees of atypia. These structures may even become detached and buried in the contracting cicatrix of the base. Newcomb found the evidences of atypical epithelial proliferation in 29 per cent of 161 chronic gastric ulcers, and Dible¹² observed them in 32 per cent of 126 ulcers. Several authors have called attention to the fact that the heterotopia and atypia of the regenerating epithelium have frequently led to an erroneous diagnosis of carcinoma. This probably accounts for the high incidence of carcinomatous degeneration of chronic peptic ulcers reported in some series.

DIAGNOSIS OF CARCINOMA

It is not within the province of this paper to discuss the criteria for the diagnosis of cancer. These depend on the usual pathologic features of anaplasia, local invasion and metastasis. As has been indicated, great care must be exercised in differentiating nonmalignant heterotopic atypical epithelium from true carcinoma.

12. Dible, J. H.: Gastric Ulcer and Gastric Carcinoma, *Brit. J. Surg.* **12**:666, 1924.

DIAGNOSIS OF ULCER-CARCINOMA

By definition, an ulcer-carcinoma of the stomach is a carcinoma which has developed secondarily in a preexisting chronic peptic ulcer. To prove this sequence of events is by no means simple.

The macroscopic examination is of little value, for it is well known that the typical gross form of chronic benign ulcer may be exactly reproduced by an ulcerated primary carcinomatous growth.

Even the characteristic microscopic features of chronic callous peptic ulcer may be duplicated in ulcerated cancer (Hauser,⁵ Stromeyer,¹⁰ Anschütz and Konjetzny,⁸ Moszkowicz,¹³ Dible¹² and Newcomb⁴). I examined 100 surgical specimens of primary gastric carcinoma and readily confirmed this fact. In addition, particular attention was paid to the relationship of the muscularis mucosae and the muscularis propria in the ulcerated carcinomas, and they were observed to be closely approximated in 3 specimens. This finding is in disagreement with Newcomb's contention that this sign is pathognomonic of *primary* peptic ulceration. The approximation of the two muscular layers appears to be merely a frequent result of chronic peptic ulceration and may therefore also be observed in a secondarily ulcerated carcinoma in which peptic digestion has proceeded to a degree to involve normal tissue and produce the typical pathologic picture of chronic peptic ulcer.

Because of the possible similarity between primary peptic ulcer and ulcerated carcinoma and the lack of a specific anatomic feature which would indicate the preexistence of a benign lesion, it seems necessary to follow the most conservative and critical criteria for the diagnosis of ulcer-carcinoma, such as were outlined by Hauser⁵ and supported by Borrmann¹⁴ and by Anschütz and Konjetzny.⁸ These criteria require that, in addition to the presence of the characteristic features of chronic peptic ulcer, the carcinoma must be localized to a narrowly circumscribed area of the margin of the ulcer while the base is entirely free of cancer or is, at least, only slightly infiltrated adjacent to the focus of origin of the tumor. This picture, of course, is seen only with the carcinoma in the earliest stage. In more advanced stages of ulcer-carcinoma, according to Spilsbury,¹⁵ the malignant cells may advance from the margin of the ulcer into the tissue of the base, where they must traverse dense connective tissue poorly supplied with blood and having a precarious

13. Moskowicz, L.: Ueber einen Fall von jungen "Ulcuscarcinom" des Magens, Virchows Arch. f. path. Anat. **253**:511, 1924.

14. Borrmann, R.: Ulkuskarzinom, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 4, pt. 1, pp. 902-917.

15. Spilsbury, B. H., and Ryffel, J. H.: The Morbid Anatomy and Histology of Gastric Ulcer, with Special Reference to Its Relationship to Cancer of the Stomach, Proc. Roy. Soc. Med. **15**:25, 1921-1922.

lymph flow; or they may grow into the normal wall of the stomach, where a loose arrangement of the tissues, abundant blood supply and a free lymph flow exist to facilitate their spread. From the knowledge of the behavior of carcinoma generally, it seems probable that such a tumor would infiltrate the surrounding healthy tissues more readily than the scar tissue in the base of the ulcer. Thus, as illustrated by Borrmann,¹⁴ the ulcer would be eccentric in relation to the area of carcinoma rather than in its center. In the advanced stages of the disease the diagnosis is extremely difficult and may even be impossible.

A critical evaluation of the criteria mentioned, however, reveals two possible sources of error. Hauser,⁵ Borrmann,¹⁴ Stromeyer,¹⁰ Anschütz and Konjetzny⁸ and others have discussed the possibility of the independent occurrence of ulcer and carcinoma anatomically close to one another in the same stomach. The two lesions, by their progressive enlargement, might finally meet and thus produce the illusion of a carcinoma arising in the edge of a chronic ulcer. As pointed out by Gömöri,⁶ however, the tumor would tend to be most voluminous at its focus of origin rather than at the margin of the ulcer. The other point to be considered in the diagnosis of ulcer-carcinoma is the possibility of the complete or almost complete ulceration of a primary new growth so that there remains little, if any, carcinomatous tissue and what little there is can be found only after careful microscopic examination (Moszkowicz,¹³ Stromeyer,¹⁰ Billroth,¹⁶ Ziegler¹⁷). Such severe destruction would probably also explain the production of the "ring" form of carcinoma, which consists of a cancer-free typical peptic ulcer base surrounded by a residual circle of neoplastic tissue (Stromeyer,¹⁰ Borrmann¹⁴). Gömöri,⁶ on the other hand, concluded that such a lesion might be a primary peptic ulcer in whose border carcinoma has developed in simultaneous multicentric foci which have fused to form a ring. As evidence in support of this theory, he presented a case in which the ring of cancer was incomplete and also cited the report¹⁸ of a similar lesion. This evidence does not appear to be conclusive, however. In view of the frequency with which extensive ulceration of gastric carcinoma is observed, it is probably more logical to account for the incomplete circle on the basis of additional destruction of a segment of the circumference of the carcinomatous ring.

In the light of these criticisms, it seems that there is a possibility that carcinoma originating in peptic ulcer may not exist. The term ulcer-carcinoma, therefore, should be used only if these considerations are borne in mind.

16. Billroth, cited by Anschütz and Konjetzny.⁸

17. Ziegler, cited by Anschütz and Konjetzny.⁸

18. Klein, E., and Demuth, F.: Zur Frage des Ulcus-Karzinoms des Magens, Beitr. z. path. Anat. u. z. allg. Path. 79:117, 1927; cited by Gömöri.⁶

MATERIAL AND METHODS

The material studied was drawn from a series of 1,057 gastrectomy specimens received in the pathologic laboratories at the Mount Sinai Hospital from January 1928 to July 1936 and from 4,400 autopsies performed during the same period. The surgical specimens were classified as shown in table 2. From the careful routine gross and microscopic examinations of this rather extensive material, a provisional diagnosis of ulcer-carcinoma of the stomach was made for 11 specimens. Ten of these were from the surgical series and 1 from the postmortem series. The evidence furnished by the routine examination was not considered sufficient for the establishment of a definite diagnosis. Consequently, these specimens were made the subject of special investigation.

The routine microscopic sections were first carefully examined. Three specimens were eliminated because they did not satisfy the criteria of ulcer-carcinoma. Two of these were considered to be ulcerated carcinomas and 1 a chronic

TABLE 2.—*Gastrectomy Material Received from Jan. 1, 1928 to July 1, 1936.*

Gastric ulcer.....	139
Gastric carcinoma.....	344
Duodenal ulcer.....	351
Healed ulcers.. {duodenal and gastric..... 1}	11
{gastric..... 3}	
{duodenal..... 7}	
Gastritis.....	59
Gastritis and erosions.....	6
Duodenitis.....	19
Duodenitis and erosions.....	8
Duodenitis and gastritis.....	18
Jejunal or gastrojejunal ulcer.....	57
Sarcoma (various types).....	22
Hodgkin's disease.....	2
Syphilis.....	1
Miscellaneous.....	10
Condition suggestive of ulcer-carcinoma.....	10
Total.....	1,057

peptic ulcer with definite atypical hyperplasia of the mucous membrane. The remaining 8 were then studied by means of the following technic:

A full size outline drawing was made of the gross specimen. The entire ulcer was then cut serially into numbered blocks, and these were accurately outlined in the drawing. Microscopic sections were cut from each block and stained with hematoxylin and eosin. Representative sections were also stained by the Van Gieson method to determine the arrangement of the muscular layers. Each section was examined for the various features of chronic peptic ulcer and for the presence of carcinoma. An outline drawing was then made of each microscopic section to show the distribution of the malignant growth. Finally, the entire lesion was reconstructed in the form of a composite relief drawing, thus demonstrating the extent of the tumor in relation to the ulcer's base, its margins and the surrounding tissues. This method was suggested by Konjetzny's¹⁹ diagrammatic illustration of 1 of his 2 reported ulcer-carcinomas.

19. Konjetzny, G. E.: Ueber die Beziehungen der chronischen Gastritis mit ihren Folgeerscheinungen und des chronischen Magenulcus zur Entwicklung des Magenkrebses, Beitr. z. klin. Chir. 85:455, 1913.

REPORT OF CASES

CASE 1.—A 33 year old woman was admitted to the surgical service of Dr. A. A. Berg. Her symptoms, which were of two years' duration, consisted of daily attacks of epigastric pain, relieved by vomiting and unrelated to the ingestion of food. The pain was constant for three days before her admission to the hospital. A gastric test meal was attempted, but the contents of the stomach were bloody. The stool gave a positive reaction to the test for occult blood. The clinical impression was that of a penetrating peptic ulcer. The patient's condition improved when she was given a Sippy diet. A series of gastric roentgenograms taken after clinical improvement revealed a penetrating lesion in the antrum of the stomach, which appeared to be benign. A subtotal gastrectomy was performed.



Fig. 1.—*A*, photograph of an ulcer-carcinoma (?). Note the typical form of chronic peptic ulcer. *P* indicates the proximal side of the specimen. *B*, photograph of a longitudinal cross section. Note the overhanging superior lip and the sloping distal margin of the ulcer. The arrow points to the sharply demarcated muscularis turned up into the edge of the ulcer.

Examination of the specimen revealed an oval ulcer 2.5 by 1.8 cm. on the lesser curvature in the antrum of the stomach (fig. 1 *A*). The proximal edge of the ulcer was overhanging, and the distal margin sloped up gradually. The base was red, and at one side the staircase appearance of the ulcer was distinct. The distal edge was rough in contrast to the smooth appearance of the mucosa on the proximal side, and at this point the mucosa was mobile whereas at the distal margin it was fixed. No lymph nodes were found in the gross specimen.

A longitudinal section of the ulcer presented the typical fish hook form of chronic peptic ulcer, and even macroscopically the muscularis could be seen turning upward into the edge of the ulcer (fig. 1 B).

Microscopically the lesion showed all the characteristic features of chronic peptic ulcer (fig. 2). A small area of carcinoma was localized at the distal margin (fig. 3). The base was free from carcinoma. Early invasion of the sub-mucosa was seen in only one block. There was considerable atypical epithelial hyperplasia of the mucosa adjacent to the carcinomatous area. In addition, two distinct areas of adenocarcinoma were noted at a little distance from the main focus. There seemed to be a gradual transition between the atypical epithelium of the hyperplastic mucous membrane and the areas of carcinoma. Microscopically several small lymph nodes were seen which were free of metastatic involvement. Figure 4 shows the final relief drawing illustrating the distribution of carcinomatous growth.

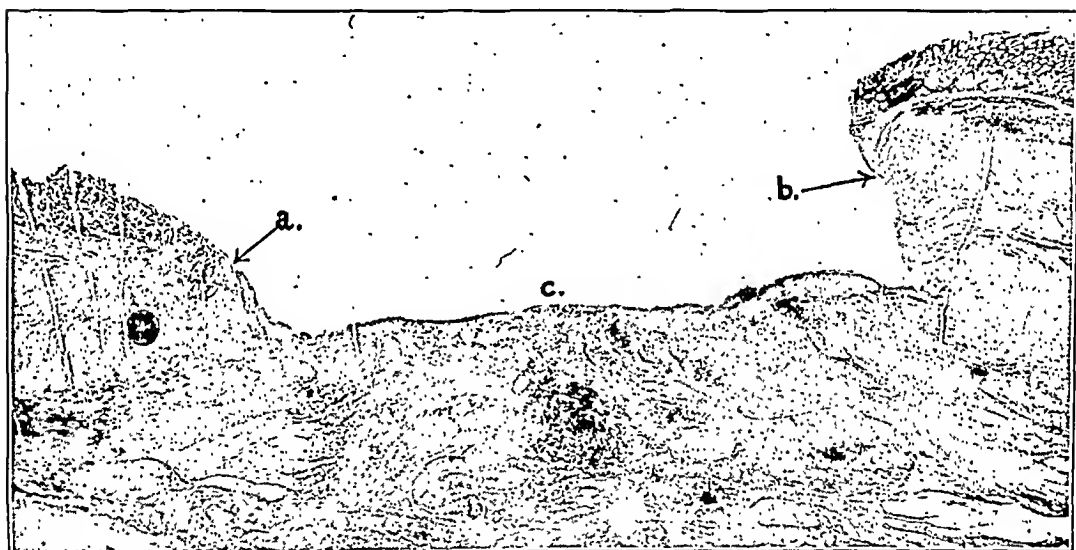


Fig. 2.—Low power photomicrograph of a section taken from the block shown in figure 1 B. Arrow *a* points to the area of carcinoma at the distal edge of the ulcer; arrow *b* indicates the fusion of the muscularis mucosae and muscularis propria, and arrow *c* marks the characteristic callous peptic ulcer base, in which the muscularis has been completely destroyed. Note the many blood vessels in the base; these show inflammatory changes.

CASE 2.—The patient was an electrician 47 years of age. His symptoms consisted essentially of postprandial epigastric pain over a period of six years, relieved by a modified Sippy diet. He was operated on at another hospital for the suture of a free perforation of a large callous ulcerated lesion of the anterior wall of the stomach in its midportion adjacent to the lesser curvature; at that time the lesion was considered to be possibly malignant. Since then, for one year, he had had postprandial pain in the epigastrium, eructations, pyrosis and occasional vomiting. The pain was relieved by the ingestion of milk and alkalis. He was admitted to this hospital under the care of Dr. A. O. Wilensky, and a subtotal

gastrectomy was performed. Considerable difficulty was encountered during the operation in separating the stomach from the liver and the pancreas, to which it was densely adherent.

The specimen presented a distorted appearance, probably because of the extensive adhesions and the previous surgical procedure. Along the inferior edge of the specimen there was infiltration with scar tissue, and there were two ulcerated areas which had probably formed one large ulcer in the intact stomach. The lesion measured 3 by 2.5 cm. The base consisted partially of adherent brownish green hepatic tissue. The margin of the ulcer was somewhat indurated by cicatricial tissue. There was thick scar tissue beneath the ulcer. On reconstruction of the specimen it was apparent that the ulcer was at the pyloric end, saddling the lesser curvature. No lymph nodes were found.



Fig. 3.—Medium power photomicrograph of the area of carcinoma indicated by the arrow in figure 2.

Microscopic examination revealed all the typical features of chronic peptic ulcer. Three distinct areas of adenocarcinoma, well localized at the ulcer margin, were found, as shown in figures 5 and 6. Evidence of early carcinomatous invasion was found in only one block.

Comment.—According to the pathologic criteria employed in this study, the lesions in cases 1 and 2 might be considered examples of chronic benign peptic ulcers which had undergone malignant degeneration. Both lesions presented all the characteristic features of chronic peptic ulcer; there were localized areas of carcinoma in the ulcer margins, and the ulcer floors were completely free of cancerous infiltration.

Nevertheless, as has been noted, these criteria are not exempt from possible criticism, for precisely similar pathologic pictures might conceivably be produced by either of two other processes, namely, the almost complete ulceration of a primary carcinoma and the independent occurrence of ulcer and carcinoma anatomically adjacent to one another, with subsequent fusion. Therefore, it must be conceded that although the lesions in these 2 cases were suggestive of so-called ulcer-carcinoma on the basis of the strict criteria employed their pathogenesis is still open to question. It does not seem possible with the morphologic evidence available to arrive at a more definite differential diagnosis at the present time.

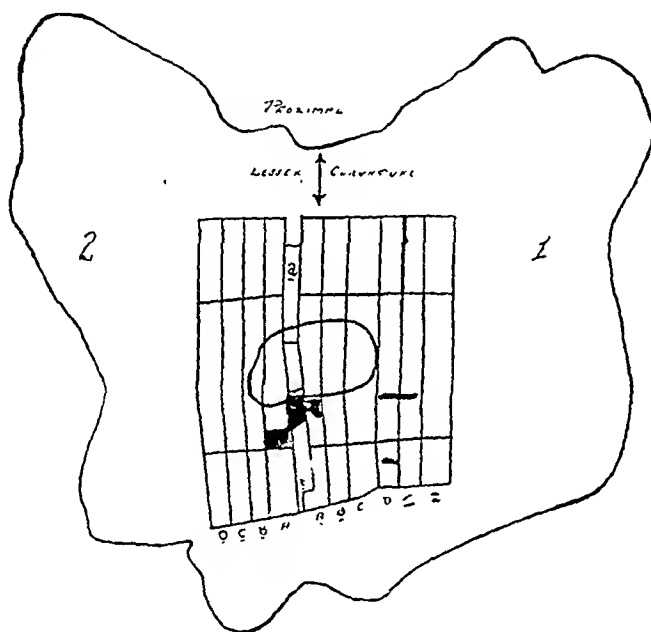


Fig. 4.—Composite relief drawing made from microscopic sections of serial blocks to show the location and extent of the carcinomatous growth. The solid black areas represent the multiple neoplastic foci. The base of the ulcer is free of cancer.

The next case is reported as an instance of the ring form of carcinoma, which has been described. In my opinion, the lesion was probably an ulcerated primary carcinoma rather than a primary ulcer with multicentric neoplastic degeneration in its borders.

CASE 3.—The patient was a 44 year old man who was admitted to the surgical service of Dr. A. A. Berg with a five year history of gastrointestinal symptoms. These consisted of periodic attacks of epigastric burning pain radiating to the right side and to the back, accompanied by epigastric distention, sour eructations and occasional vomiting. The pain appeared about two hours after each meal and was relieved by the ingestion of food and of alkalis. The attacks would

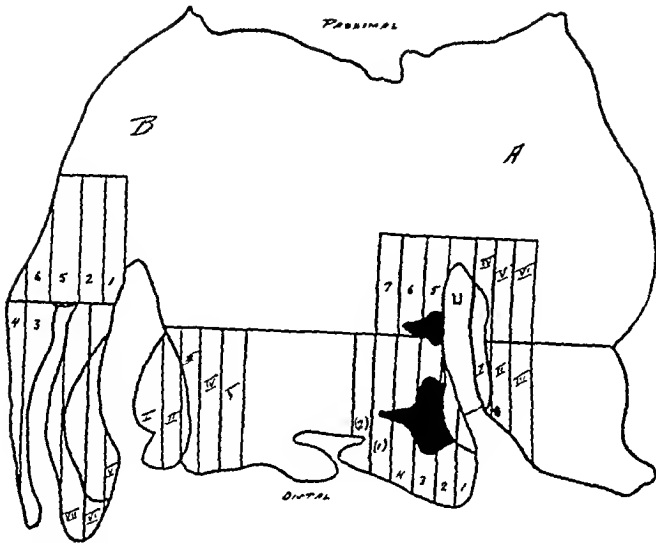


Fig. 5.—Ulcer-carcinoma (?). Composite relief drawing showing localized area of carcinoma at the ulcer margin. Note the multiple foci of neoplastic growth, represented by the solid black areas. The ulcer base is uninvolved. The unusual gross picture is due to cicatricial distortion and contraction of the specimen by fixation in solution of formaldehyde.

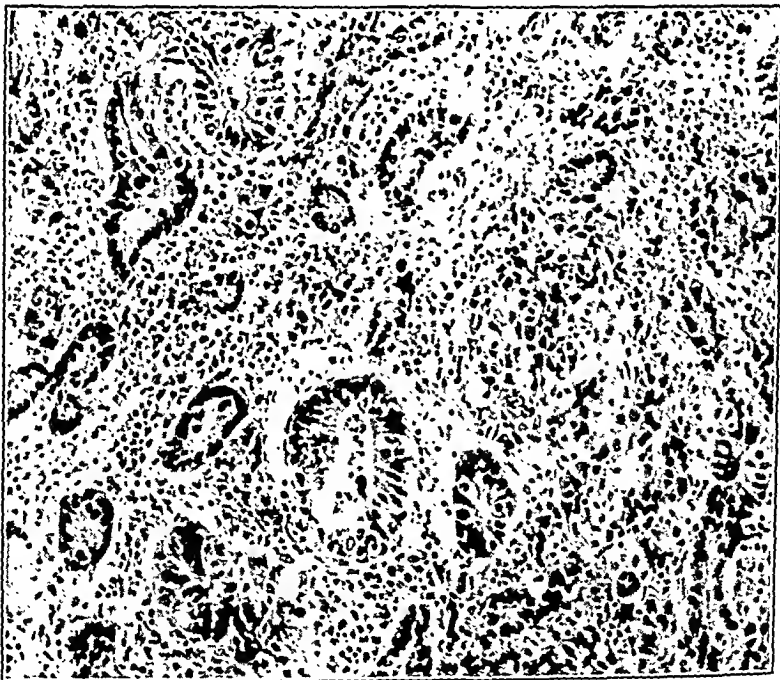


Fig. 6.—High power photomicrograph showing carcinoma.

occur over a period from two to four months and a free interval of a few months would follow. A liberal Sippy diet during the past two years more or less controlled the symptoms, which, however, recurred after dietary indiscretion. One year prior to his admission he was examined at another institution. The Ewald test meal disclosed a free acid content of 92 per cent and a total acid content of 104 per cent. The gastrointestinal roentgen examination at this time showed a widened pyloric interval and a small penetrating lesion in the prepyloric region on the lesser curvature of the stomach. The diagnosis was pyloric ulcer and penetrating gastric ulcer on the lesser curvature of the stomach. Roentgen examination two weeks before admission to this hospital revealed a narrowing in the prepyloric region which was suggestive of a neoplasm.

On his admission, the stool gave a positive reaction to the guaiac test for occult blood. The Rehfuess test meal revealed bloody gastric contents which showed a maximum free acid content of 44 per cent and a total acid content of 68 per cent.

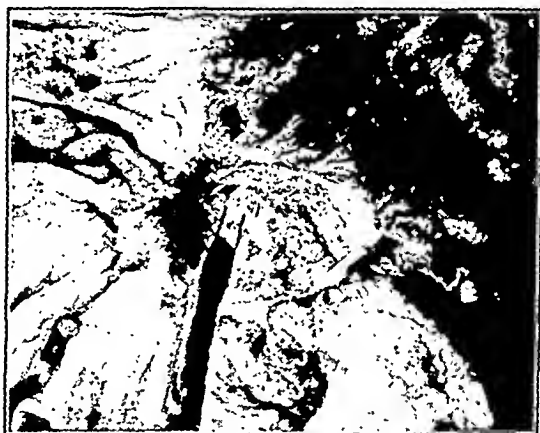


Fig. 7.—Photograph of a "ring form" carcinoma. Note the typical form of chronic peptic ulcer.

Roentgen examination of the stomach at this time showed an irregular constriction of the antrum, extending from the pylorus approximately to the reentrant angle. There seemed to be a large ulcer within the lesion. There was slight delay in gastric motility. These findings suggested an ulcerating lesion in the antrum of the stomach, which was considered to be probably malignant. A subtotal gastrectomy was performed.

Examination of the specimen revealed a crater-like ulcer 2.5 cm. in diameter on the lesser curvature of the antral portion of the stomach (fig. 7). There was penetration of the layers of the stomach wall for 1 cm. The mucosa around the edge of the ulcer was fairly easily movable over the deeper layers, and there was no heaping-up of the mucous membrane.

Microscopic sections showed all the characteristic features of chronic peptic ulcer and, in addition, a carcinomatous growth distributed as shown in figure 8. The question mark in block II B4 indicates the area in which the mucosa was absent at the edge of the ulcer because of a technical error. From the entire picture, however, it was considered probable that the ring of carcinoma was complete.

The following 2 cases are presented to illustrate the occurrence of typical chronic peptic ulceration in a primary carcinoma and the value of the serial block examination in the differential diagnosis of gastric ulcers.

CASE 4.—A man 42 years of age was admitted to the surgical service of Dr. R. Lewisohn. His illness began eighteen months prior to admission, with symptoms of epigastric pain and abdominal distention which occurred one and one-half to two hours after each meal and were readily relieved by the use of sodium bicarbonate and by the ingestion of milk and cream. There was mild anorexia,

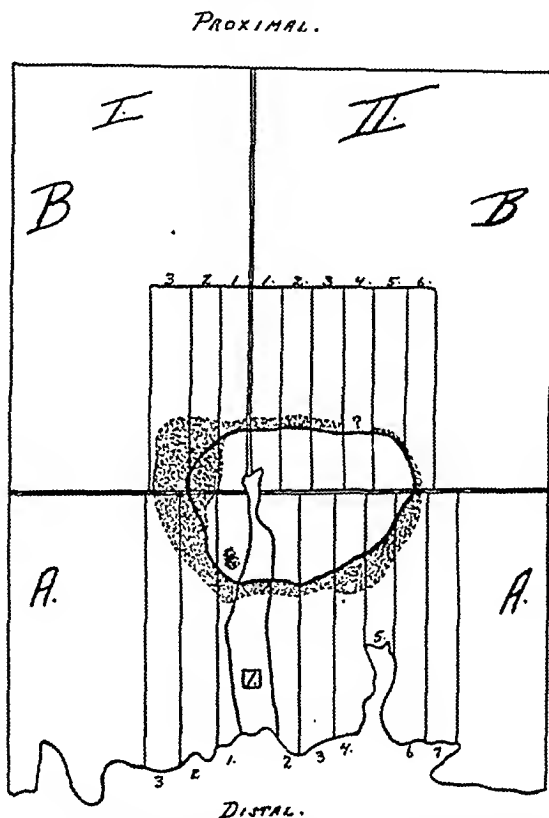


Fig. 8.—Composite relief drawing showing the "ring form" of carcinoma. The stippling represents malignant growth. The base of the ulcer shows only slight carcinomatous infiltration.

and he vomited on several occasions. For six months his diet was restricted almost exclusively to milk and cream administered every one to two hours. This resulted in only partial relief of pain.

Roentgen examination of the stomach two weeks before admission revealed the presence of a niche at the reentrant angle. The vomitus gave a strongly positive reaction to the guaiac test for occult blood. The Wassermann test was negative. The clinical diagnosis was chronic peptic ulcer of the stomach. At operation, a deeply penetrating ulcer above the reentrant angle was found, and a subtotal gastrectomy was performed.

The opened stomach presented a large oval ulcer saddling the lesser curvature 5 cm. above the pyloric ring (fig. 9*A*). The defect measured 2 by 2.5 cm. Its margins were smooth and had a punched-out appearance, and its base was deep, extending into the gastric wall for 1.25 cm. Macroscopically the surrounding mucous membrane did not appear abnormal. In the longitudinal section the fish hook shape was noted, and even with the naked eye the upturning of the muscularis into the base of the ulcer could be seen (fig. 9*B*).

The first block taken for microscopic section was cut along the midline of the lesion and measured 6.25 cm. in length (fig. 10). The base and margins of the ulcer showed all the characteristic features of chronic peptic ulcer, including the approximation of the muscularis mucosae and the muscularis propria. The

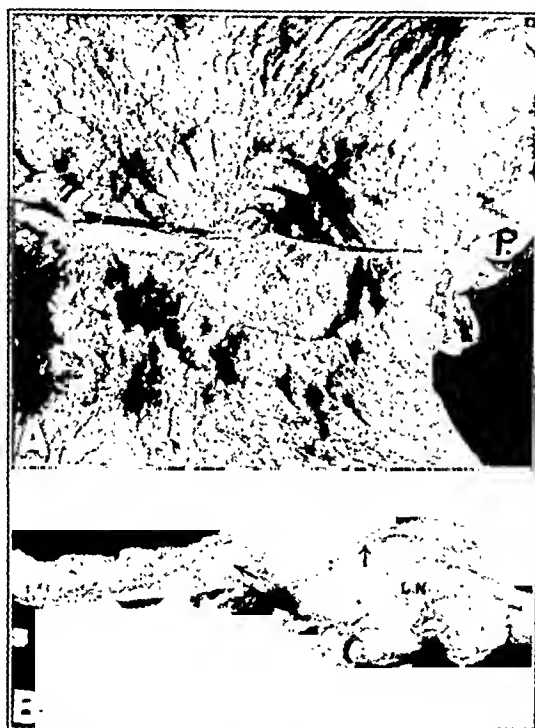


Fig. 9.—*A*, photograph of an ulcerated carcinoma. Note the typical form of chronic peptic ulcer. *P* indicates the proximal side of the specimen. *B*, photograph of a longitudinal cross section, showing the typical form of chronic peptic ulcer. Arrows point to the sharply demarcated muscularis turned into the ulcer margin. (Note the similarity to the section in figure 1*B*). *L.N.* indicates a lymph node involved by metastatic carcinoma.

mucous membrane of the superior segment of the block was completely involved by adenocarcinoma. The base of the ulcer was free of tumor except in the area just adjacent to the superior border, where there was slight infiltration. The mucous membrane of the distal segment presented epithelial proliferation, with cellular atypia and several small islands of carcinoma cells. A lymph node present in the section showed advanced metastatic involvement.

From this block a provisional diagnosis of ulcer-carcinoma was ventured. However, complete examination of the ulcer and the surrounding area by the

serial block technic proved the lesion to be obviously a primary carcinoma which had undergone typical peptic ulceration (fig. 10).

CASE 5.—A man 70 years of age was admitted to the medical service of Dr. G. Baehr. He had had epigastric pain and gaseous eructations, relieved by the use of alkalis, for five years and "cigaret cough" for several years. Two weeks before admission he began to notice severe epigastric pains after eating and also during the night, and he vomited several times. He lost several pounds during one year.

On admission, he was thin and pale. The stool gave a positive reaction to the guaiac test for occult blood. The Rehfuess gastric test meal disclosed a maximum free acid content of 40 per cent and a total acid content of 56 per cent. A series of gastrointestinal roentgenograms revealed a persistent prepyloric defect involving principally the side of greater curvature of the stomach. There was delay in gastric motility, evidenced by a 30 per cent residue in the stomach after six hours

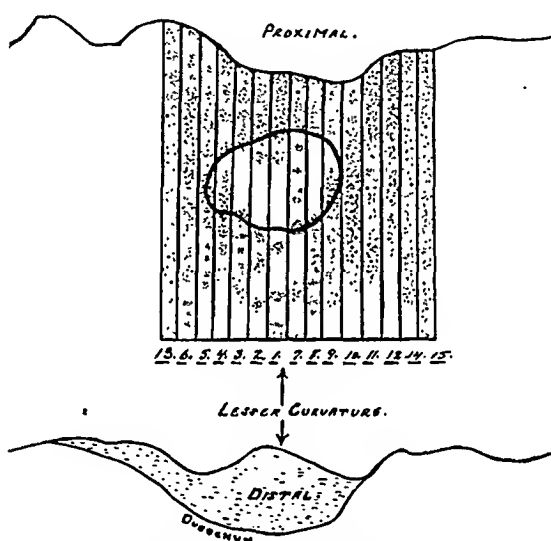


Fig. 10.—Composite relief drawing showing the wide distribution of the carcinomatous infiltration, represented by the stippling.

and moderate residue after twenty-four hours. It could not be stated definitely whether this prepyloric defect was due to the presence of an old chronic ulcer or whether it was malignant. However, the clinical history seemed to favor the diagnosis of chronic ulcer.

The patient's poor general condition precluded operation at this time, and he was given a Sippy diet. Under this regimen he was free of pain and was sent home to continue this treatment.

He was readmitted to the hospital several days later, acutely ill, dehydrated and emaciated, with a temperature of 103 to 104 F. The blood culture yielded *Bacillus coli*. The patient died four days later.

At autopsy there was observed an infiltrating squamous cell carcinoma of the right main bronchus with metastases to the regional lymph nodes, bronchopneumonia, pleuropericarditis and mediastinitis. In addition, there was a gastric lesion which was situated on the lesser curvature of the stomach 1 cm. proximal to the pyloric ring. It consisted of a large oval ulcer measuring 5 by 3 cm. (fig. 11 A).

The upper and lateral edges were slightly hemorrhagic, rounded and somewhat undermined. The distal edge was distinctly piled up and was more prominent than the remainder of the ulcer margin. The border here sloped gradually to a finely granular base. A section of this piled-up edge revealed uniformly gray tissue 1 cm. in thickness. The serosa at the site of the ulcer showed no changes. Macroscopically the gastric lymph nodes appeared normal.

Histologic examination of the original sections (*O* and *O'* in figure 11 *B*) led to the provisional diagnosis of ulcer-carcinoma. In section *O* there was a localized area of adenocarcinoma at the margin of the ulcer. There was also a partial adjacent infiltration of the base. Both of these carcinomatous areas showed all

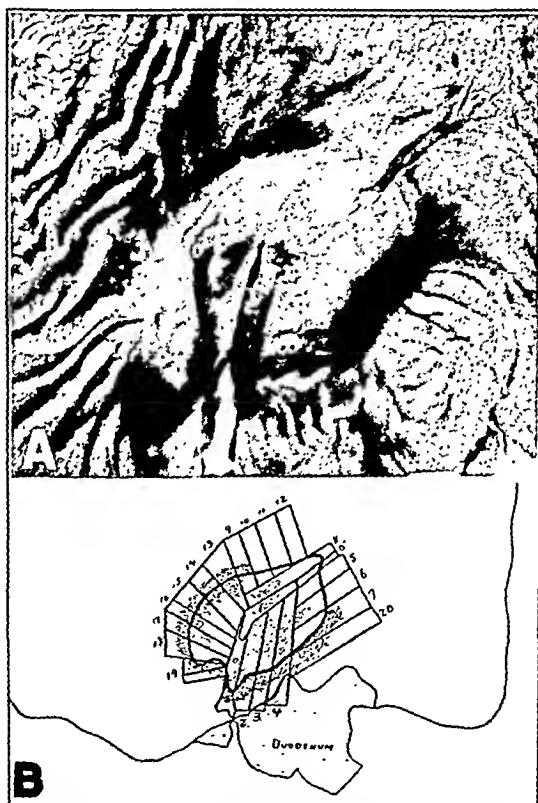


Fig. 11.—*A*, photograph of an ulcerated carcinoma. Note the typical form of chronic peptic ulcer. *B*, composite relief drawing showing the extent of the carcinomatous growth, represented by the stippled area.

the characteristic features of chronic peptic ulcer. Section *O'* was typical of peptic ulcer and was also entirely free of carcinoma. Sections examined by the serial block technic, however, revealed widespread carcinomatous infiltration of the base and borders of the ulcer, except in blocks 5, 10, 11, and 12. Microscopically the lymph nodes showed no metastatic involvement.

On the basis of the criteria previously discussed it is impossible to state definitely whether this lesion was an advanced ulcer-carcinoma or an eccentrically ulcerated carcinoma. The latter diagnosis is considered more probably correct, because were the growth an advanced ulcer-carcinoma one would expect in this

stage of growth much more widespread carcinomatous invasion of the adjacent stomach wall, commensurate with the degree of involvement of the base of the callous ulcer.

Of the remaining 3 lesions which were studied by the serial block method, 2 proved to be ulcerated carcinomas and 1 a benign ulcer with atypical epithelial hyperplasia.

SUMMARY AND CONCLUSIONS

The criteria for the diagnosis of so-called ulcer-carcinoma are discussed and evaluated.

The characteristic pathologic features of chronic benign peptic ulcer may be exhibited in every detail by primary gastric carcinoma which has undergone peptic ulceration.

There is no one pathologic feature which may be considered pathognomonic of the preexistence of a chronic benign peptic ulcer.

A serial block method for the complete anatomic study of gastric ulcerations is described.

In a series of 141 cases of chronic gastric ulcer and 353 cases of gastric carcinoma there were but 2 cases in which the diagnosis of ulcer-carcinoma could be suggested on the basis of certain pathologic criteria.

The diagnosis of ulcer-carcinoma, even though based on the strictest available criteria, may still be open to criticism.

It is concluded that malignant degeneration of chronic gastric ulcer, if it occurs at all, is rare.

Because of the rarity of proved ulcer-carcinoma, there is insufficient justification for early radical surgical treatment of gastric ulcer based on the possible danger of malignant degeneration.

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SPONDYLOLISTHESIS

TREATMENT BY ANTERIOR BONE GRAFT

KELLOGG SPEED, M.D.

CHICAGO

Although somewhat confusing and laborious, a detailed study of the human spine must be the basic factor in an understanding of certain of its clinical disorders. The one selected for discussion here is spondylolisthesis, a condition or anomaly formerly mentioned only as occurring in women because of its relation to maternal dystocia. Recent investigation has sought the cause of pain and disabilities affecting the lower part of the back, which result in difficulties in awarding compensation when the condition is directly associated with the traumas of occupation or when distress and restricted activity are chronically prolonged exclusive of a known trauma. In the course of this investigation the condition and its alleviation have become prominent in surgical research. The advent of high grade roentgenologic aid in the clinical study of the human spine has added to knowledge of the anatomic and pathologic character of these formerly obscure conditions affecting the vertebrae. For decades anatomic research has been undertaken in this subject, but it has not been well coordinated with clinical records describing the nature of the complaint and the results of examination. The studies of Dwight, Willis, Kilian, Neugebauer, Rosenberg, Goldthwaite, Lord and others have received scant attention from the clinical surgeon, whose interest in the fascinating study of the spine was perhaps finally aroused by Schmorl's intensive research on his vast anatomic collection.¹

Spondylolisthesis was first named by Kilian in 1852, but it had been described by Herbineau in 1782, Rokitansky in 1839 and Belloc in 1849. After Neugebauer's published report of 101 cases in 1892, largely composed of observations on museum specimens, attention to the subject slumped, although isolated instances of operative treatment

1. Schmorl, G.: *Archiv und Atlas der normalen und pathologischen Anatomie in typischen Röntgenbildern. Die gesunde und kranke Wirbelsäule im Röntgenbild: Pathologisch-anatomische Untersuchungen*, Leipzig, Georg Thieme, 1932, p. 182.

appeared, such as that of Ryerson, in 1915.² A most satisfying study of the lumbosacral part of the spine formed a part of Theodore A. Willis' thesis at Western Reserve University in June 1922.³ He assumed a normal vertebral formula of seven cervical, twelve thoracic, five lumbar, five sacral and four coccygeal segments, with variations. The cervical vertebrae remain approximately constant; the coccygeal segments may vary but are of negligible importance on account of their vestigial nature.⁴ The greatest clinical interest lies in the thoracolumbar group, which may be associated with phylogenetic changes affecting the progression or retrogression of the leg on the spinal column in the change from pronograde to orthograde ambulation.⁵ This thoracolumbar group must be considered as a unit. Willis stated that variation in the number of lumbar vertebrae is often found to be coincident with or compensated by a reverse variation in the thoracic group, the total number of presacral segments remaining unchanged. The modal number of human thoracolumbar vertebrae is seventeen; and of 748 columns examined by Willis only 5 showed sixteen and 26 showed eighteen. The remaining 772 showed the modal number, the numerical stability of the presacral segments being 95.8 per cent.

A definition of spondylolisthesis was given by Ziegler:⁶ "It is a deformity in which by the action of the weight of the trunk, the body of the 5th lumbar vertebra and the portion of the spinal column above it slip forward over the base of the sacrum." The term means slipping vertebra. In true spondylolisthesis the arch of the fifth lumbar or other vertebra concerned, with its spinous process, does not take part in the spondylolisthesis, the anterior part or body of the vertebra alone being displaced. If the whole vertebra is set forward, lifted over the hump of the supporting facets on the base of the sacrum, the condition is known as pseudospondylolisthesis and represents a true dislocation or subluxation. Schmorl found among the spines in his material 46 instances of true spondylolisthesis (25 in women and 21 in men) and 14 of pseudospondylolisthesis (11 in women and 3 in men).

The cause for separation of the neural arch or its isthmus may be either traumatic violence, usually a shearing strain resulting in fracture, or anomalies of development in the laminae or isthmus, the inter-

2. Ryerson, E. W.: Recurrent Spondylolisthesis with Paralysis: Bone-Splint Transplantation, *J. A. M. A.* **64**:24 (Jan. 2) 1915.

3. Willis, T. A.: Lumbo-Sacral Vertebral Column in Man: Its Stability of Form and Function, *Am. J. Anat.* **32**:95 (July) 1923.

4. Mitchell, G. A. G.: Significance of Lumbosacral Transitional Vertebrae, *Brit. J. Surg.* **24**:147 (July) 1936.

5. Paterson, A. M.: The Human Sacrum, *Proc. Roy. Soc. Med.* **51**:520, 1892.

6. Ziegler, E.: *Lehrbuch der allgemeinen und speciellen pathologischen Anatomie für Aerzte und Studierende*, ed. 9, Jena, Gustav Fischer, 1898, sect. 4, p. 219.

articular part of the neural arch, but generally is a failure of bony fusion, well described by Neugebauer in 1892.⁷ Inflammatory reactions affecting predominately this area may possibly influence the separation of the arch. Constriction lines of the isthmus were noticed by Poirier,⁸ and a definite division of the lamina was reported by Shore⁹ in 1929 in an African native woman. In the same year, Brailsford,¹⁰ after roentgen examination of more than 3,000 backs, found only 5 instances of spondylolisthesis, of which 3 were in girls 13, 15 and 17 years of age, 1 in a boy of 17 and 1 in a man of 35. He reviewed the 5 cases reported by Turner and Tchirkin¹¹ and considered that only 1 of the group was an instance of real spondylolisthesis. Hibbs and Swift,¹² reporting operation on 23 patients in group III of their compilation found forward displacement of the 5th lumbar vertebra varying from $\frac{1}{4}$ inch (0.6 cm.) to the full width of the corpus, along with a separation of the laminae and loss of the bony anchorage which would prevent the fifth lumbar vertebra and the superimposed spine from slipping forward. The ages of the patients varied from 15 to 51; 15 were men and 8 were women. The percentage of their cases in which there was a history of trauma was 47.8. Some separations of the isthmus may represent fractures sustained in childhood, unrecognized until strain in adult life produces symptoms following either a slow or a sudden slipping forward of the vertebra. There is no doubt that the isthmus, as described by Chandler¹³ and others, is a vulnerable area of incomplete ossification which may permit many of these displacements.

When the neural arch of the fifth lumbar vertebra is unfused or separated, there may follow sooner or later a change in the axis of

7. Faldini, C.: Osservazioni cliniche e radiografiche sopra la spondilolistesia e la spondilolisi, *Chir. d. org. di movimento* **12**:545 (Sept.) 1928. Lane, W. A.: Spondylolisthesis, *Tr. Path. Soc. London* **36**:364, 1885. Lange, M.: *Die Wirbelgelenke: Die röntgenologische Darstellbarkeit ihrer krankhaften Veränderungen und ihre Beziehungen zu den verschiedenen Erkrankungen der Wirbelsäule*, ed. 2, Stuttgart, Ferdinand Enke, 1936, p. 80. Le Double, A. F.: *Traité des variations de la colonne vertébrale de l'homme*, Paris, Vigot-Frères, 1912, p. 314.

8. Poirier, P., and Charpy, A.: *Traité d'anatomie humaine*, ed. 3, Paris, Masson & Cie, 1911, vol. 1, p. 171.

9. Shore, L. R.: Report of a Specimen of Spondylolisthesis, *Brit. J. Surg.* **16**:431 (Jan.) 1929.

10. Brailsford, J. F.: Deformity of the Lumbo-Sacral Region of Spine, *Brit. J. Surg.* **16**:562 (April) 1929.

11. Turner, H., and Tchirkin, N.: Spondylolisthesis, *J. Bone & Joint Surg.* **7**:763 (Oct.) 1925.

12. Hibbs, R. A., and Swift, W. E.: Developmental Abnormalities at the Lumbosacral Junction Causing Pain and Disability: Report of One Hundred and Forty-Seven Patients Treated by the Spine Fusion Operation, *Surg., Gynec. & Obs.* **48**:604 (May) 1929.

13. Chandler, F. A.: Lesions of "Isthmus" (Interarticularis) of Laminae of Lower Lumbar Vertebrae and Their Relation to Spondylolisthesis, *Surg., Gynec. & Obst.* **53**:273 (Sept.) 1931.

support of this vertebra on the sacrum. The upper borders of the superior articular surface of the sacrum were likened by Willis to the peak of a roof, one side formed by the base of the sacrum, which in an erect person presents an inclination of 45 degrees with the long vertical axis of the spine. The body of the fifth lumbar vertebra rests on this surface with the interposition of a wedge-shaped intervertebral disk, the broadest diameter of which lies anteriorly. The weight of the torso, head and arms must be supported on this precarious inclined surface held by the anchoring, hooklike inferior articular processes of the fifth lumbar vertebra engaged over the superior articular processes of the sacrum like a fireman's ladder. A large proportion of active support lies in the spinal muscles and some in the lumbosacral and interspinal ligaments, but there are times of relaxation or moments of strain when these sustaining factors are greatly lowered in value and the bony parts must take on a greater share of the support of the superimposed spine and torso as a whole. If a laminar (isthmian) defect is then encountered, the anteroposterior stability of the lumbosacral articulation is further endangered, and the column as a whole tends to slip downward and forward along the inclined plane of the superior surface of the sacrum.

Muscular fatigue, temporary overstrain and possible defective ligamentous support and bony anchorage readily explain spondylolisthesis. A unilateral defect in the lamina may not permit sufficient separation for this slipping, but weakness of one side of the neural arch may favor easy fracture of the opposite side or lead to favoring muscular and ligamentous relaxation. Usually the bony defect has been found to be bilateral. True spondylolisthesis will thus be almost impossible in the face of normal inferior articular processes and laminae of the fifth lumbar vertebra holding a normal relation with the sacrum. It is possible for the spine to sustain sufficient trauma, especially when flexed forward, rarely when hyperextended, to tear the inferior articular processes away from their attachments so as to let them ride up over the superior articular processes of the sacrum, an accident which causes pure dislocation. In this displacement, because the laminae and spinous process would go along with the corpus of the vertebra, pressure on the cauda or spinal nerves with resulting paralysis or lesions of the nerves may follow. Fracture of the laminae must be a simpler process in such an injury than a lifting over the obstacle of the sacral processes of all the weight above, held by strong, inelastic ligaments. Without bony lesion, the condition becomes pseudospondylolisthesis.

Following the forward displacement of spondylolisthesis must come easy tire in the lumbosacral area, pain, sometimes referred down both thighs and buttocks, stiffness in the back at that level, shortening of the spine, a crease across the back at or near the level of the iliac crests, a

palpable depression over the fifth or fourth lumbar vertebra and increase of lumbar lordosis. The abdomen becomes proportionately protuberant, and the gait may become waddling. A final proof of the diagnosis lies in the roentgenograms, the posteroanterior view showing the overlying shadow of the sacrum on the body of the fifth lumbar vertebra and the lateral view the projection forward of the fifth body and possibly the defect in the laminae. An ancient displacement will always show a liplike projection of new bone extending anteriorly from the superior surface of the visceral border of the sacrum, formed to help sustain the body of the fifth lumbar vertebra in its new position, unless the displacement has been so complete that the centrum of the fifth lumbar vertebra comes to lie completely displaced downward in front of the sacrum. Rarely the displacement is also lateral or has an acute scoliotic angle. In 12 of 18 instances of spondylolisthesis reviewed by Chandler the condition had an acute traumatic onset, and in 6 it followed repeated strains. The laminar defects generally involve the fifth lumbar vertebra alone but may include the fourth or, rarely, involve the fourth alone. In his report, Meyerding¹⁴ mentioned one subluxation of the third on the fourth lumbar vertebra. The term spondylolisthesis is given also to any forward slipping at any level of the vertebral column accompanied by a laminar defect, whether congenital or acquired. Examples in the cervical and the dorsal region have been recorded. Other congenital or developmental defects may be present with this slipping. Spina bifida occulta is the one most frequently found, making up about 20 per cent.¹⁵ Sacralization of the transverse process of the fifth lumbar vertebra, unilateral or bilateral, old osteoarthritis and local bone sclerosis, often mistaken for Paget's disease, may be present. In Meyerding's series of cases there were 71 per cent men and 29 per cent women suffering from this affliction.

The treatments offered are of interest after this brief investigation of cause and pathogenesis. In many instances spondylolisthesis is symptomless until aggravated by trauma. Treatment may be palliative for mild involvement, when an arrest of progressing deformity is desired, or it may be curative. The first consists of traction on head and feet in a position of recumbency. The feet are elevated to an angle of 35 or 40 degrees with the torso and subjected to all the traction they can withstand, counteraction being made on the head and beneath

14. Meyerding, H. W.: Spondylolisthesis, *Proc. Staff Meet., Mayo Clin.* 9:666 (Oct. 31) 1934; *Diagnosis and Roentgenologic Evidence in Spondylolisthesis*, *Radiology* 20:108 (Feb.) 1933; *Spondylolisthesis*, *Surg., Gynec. & Obst.* 54:371 (Feb. 15) 1932; *J. Bone & Joint Surg.* 13:39 (Jan.) 1931.

15. Putschar, W.: Changes in the Intervertebral Discs in Spondylolisthesis and Related Conditions of the Spine, *Arch. Path.* 24:270 (Aug.) 1937. Stewart, T. D.: Spondylolisthesis Without Separate Neural Arch (Pseudo-Spondylolisthesis of Junghanns), *J. Bone & Joint Surg.* 17:640 (July) 1935.

the axillas to pull the torso in the opposite direction. This procedure may effect partial reduction, especially after a recent gross displacement or even after several months, as in Jenkins' case.¹⁶ He had his patient while lying in traction push down on the pelvic brim with his hands. The Sinclair net bed used in the treatment of fractures resulting from gunshot wounds in the femur or pelvis is an admirable means for this traction. If a reduction in whole or part can be effected, the patient may then be encased in plaster of paris, a double spica extending from the axillas to include both legs, for six or eight weeks. The cast may be followed by a steel back support in the corrected position. If the roentgenologic findings show the formation of much new bone about the lumbosacral junction, with no hope of reduction, traction may be omitted and the patient's back supported in a steel spinal brace in an attempt to prevent further displacement and to relieve fatigue.

For curative treatment, posterior spinal fusion has been done. Both the Hibbs and the Albee¹⁷ method, with or without bone transplanted from the iliac crest or the tibia, have been employed. Many patients have obtained symptomatic relief, at least for a time, by these methods of posterior spinal fusion; whether this was permanent only years of observation and close follow-up could determine. Some operations have failed to relieve the pain and back fatigue.¹⁸ Hibbs reported:

	Number of Operations	Percentage
Entirely relieved	16	66.7
Improved	3	12.5
Unimproved	5	20.8

Mathieu and Demirleau¹⁹ advised an extensive osteosynthesis of the anterior segment of the lumbar vertebrae with the iliac bone, grafts from the ilium to the sacrolumbar bone on each side being used. With it is combined intervertebral and sacral synthesis, obtained by means of a sufficiently large graft to bridge through the posterior iliac crest into the transverse processes of the lumbar vertebra. Two grafts are used on each side, one reaching into that part of the fifth lumbar vertebra which is sliding (corpus) and the other extending from the ilium to the transverse process of the fourth lumbar vertebra to solidify that connection. The authors believe that these multiple arthrodeses combined with lumbosacral arthrodesis make ligamentous pull and resulting strain impossible. This is even a more extensive procedure than Chan-

16. Jenkins, J. A.: Spondylolisthesis, *Brit. J. Surg.* **24**:80 (July) 1936.

17. Albee, F. H.: Spondylolisthesis, *J. Bone & Joint Surg.* **9**:427 (July) 1927.

18. Hellström, J.: Zur Kenntnis der operativen Behandlung von Spondylolisthese, *Acta orthop. Scandinav.* **7**:143, 1936.

19. Mathieu, P., and Demirleau, J.: Traitement chirurgical du spondylolisthésis douloureux, *Rev. d'orthop.* **23**:352 (July) 1936.

dler's trisacral fusion, done from the posterior aspect of the spine. In the reproduced films of a patient on whom the operation Mathieu described was performed, the transplants do not seem large or sturdy enough to insure permanent immobilization, and on one side the transplant extending to the transverse process of the fourth lumbar vertebra does not seem bony united. Hibbs and Swift stated: "It seems obvious that an operation which will produce strong bone fusion between the fourth and third lumbar vertebra and the sacrum is the logical procedure to employ in order to give stability to such a spine."

In 1932 Capener²⁰ reviewed this subject, including a study of 34 patients, and then suggested that the ideal fixation of the spine, mechanically efficient, would be one fixing the *body* of the fifth lumbar vertebra to the sacrum. However, if inserted transversely from the posterior aspect of the spine forward to form a supporting buttress of bone or bridge into the body of the fifth lumbar vertebra, it must go blindly and would probably injure the cauda. The attempt did not seem feasible, and his own words were: "The technical difficulties of such a procedure, however, preclude their trial." In July 1936 Jenkins recorded his case in New Zealand in which after reduction by traction he inserted a bone graft from the anterior surface of the body of the fifth lumbar vertebra into the sacrum after opening the abdomen. A successful result was obtained. In June 1933, Burns²¹ reported a similar case of a boy of 14 who was operated on at St. Georges' Hospital and had an uneventful convalescence. In his brief report he mentioned that he did not believe that the intervertebral disk is an ideal place for the bone graft and said that if in his case the graft were to become absorbed he would in his next attempt employ a steel pin! Later (September 1936) appeared Mercer's²² article describing his method of operative treatment of spondylolisthesis by an osteotomy of the lumbosacral junction from an anterior intra-abdominal approach. He stated that it was his practice to remove some or all of the intervertebral disk and bony surface, which he replaced by a two piece bone graft obtained from the patient's ilium. The patient was operated on while lying in a posterior plaster of paris shell prepared beforehand so that he could not be hyperextended while being moved and the bone grafts thus permitted to fall out of place.

In attempts at curative treatment by the support of new bones and osteosynthesis, it must not be overlooked that the principal causes of

20. Capener, N.: Spondylolisthesis, *Brit. J. Surg.* **19**:374 (Jan.) 1932.

21. Burns, B. H.: Two Cases of Spondylolisthesis, *Proc. Roy. Soc. Med.* **25**:571 (Feb.) 1932; Operation for Spondylolisthesis, *Lancet* **1**:1233 (June 10) 1933.

22. Mercer, W.: Spondylolisthesis, with Description of New Method of Operative Treatment and Notes of Ten Cases, *Edinburgh M. J.* **43**:545 (Sept.) 1936.

pain and acute displacement are at least three: (1) lifting heavy weights, (2) falling, especially on the buttocks, and (3) falls of heavy weights on the shoulders and back. The tilting of the sacrum may not be such an important factor in this mechanism because lordosis of the spine may not be present at the beginning of the act or trauma. In lifting a weight, for instance, a man starts with the hips flexed and the lumbar portion of the spine arched backward, but, as explained by Armitage Whitman, elevation of the load is carried out by use of the gluteus muscles. This action results in extension of the hips, during which the sacrum is actively tilted backward and forced against the laminae of the fifth lumbar vertebra. Lordosis is therefore absent at the start of the action but appears later, secondary to displacement at the lumbosacral joint. The upper surface of the sacrum is rotated into a nearly vertical position and carries with it the spinous process of the fifth lumbar vertebra. Capener stated the belief that this is the overlooked factor whereby the upper and posterior borders of the sacrum act as the apex of a wedge, which is driven upward and splits the fifth lumbar vertebra into two parts at the site of the congenital nonunion. Thus spondylolysis is initiated and spondylolisthesis or slipping follows.

On the basis of these findings a posterior bone graft or spinal fusion appears mechanically inefficient in attempts at cure. Even if the sacral surface, the split lumbar vertebra—posterior portion—and the lumbar spines and laminae above are locked together, it does not necessarily mean that the anterior part of the fifth lumbar vertebra (corpus and supporting facets) may not plunge farther forward and rotate down in front of the sacrum as time advances. An additional factor in favor of the anterior placing or wedging of the bone graft is found in the presence of spina bifida occulta in nearly 20 per cent of the cases, militating against a good sacral attachment of the posterior graft.²³ Nature apparently tries to limit the forward displacement of the fifth lumbar vertebra by building up a bony buttress along the anterior margin of the base of the sacrum. Thus is supplied an aid to the iliolumbar ligaments in stopping the rotation downward and obtaining a natural arrest of the slipping. Why not then implant the autogenous bone at a proper angle to penetrate the body of the fifth lumbar vertebra, traverse its intervertebral disk if necessary and engage well into the upper sacral segment? New fusion should follow to lock the whole bony together. It appears that this method might suffice and that osteotomy with removal of the intervertebral disk, favored by Mercer, would be a little too extensive and possibly unneeded in the average case. Nailing with

23. Congdon, R. T.: Spondylolisthesis and Vertebral Anomalies in Skeletons of American Aborigines, with Clinical Notes on Spondylolisthesis, *J. Bone & Joint Surg.* **14**:511 (July) 1932. Kleinberg, S.: Traumatic Spondylolisthesis. *Arch. Surg.* **3**:102 (July) 1921.

a steel pin without performing osteotomy or freshening the surface of the bone would not positively insure bony fusion, although the pin might hold longer than an autogenous bony transplant. There is, however, by this method a smaller opening and less freshening of the bony surfaces to permit irritation, extravasation of blood and formation of new bone.

TECHNIC OF THE OPERATION

An attempt may be made by suspension traction in bed to overcome some of the displacement of the fifth lumbar vertebra, depending on the duration of the condition and the roentgenologic findings.

An abdominal incision, midline umbilicus to pubis, permits full exposure of the sacral promontory after the patient is tilted back and the intestines are packed away. The promontory is palpated, and the exact condition and extent of rotation of the fifth lumbar vertebra are determined in order to confirm the roentgenologic findings. If the bifurcation of the aorta is low, it may, along with the left common iliac vein, be gently held back by a padded retractor. The peritoneum over the fourth interspace down to the sacrum is incised just to the right of the midline, and an effort is made to avoid the midsacral nerve and artery and the ganglia of sympathetic nerves. If the artery bleeds, it must be tied. The amount of displacement and angulation having been decided, a chisel is used to make an entrance into the vertebral bony mass at or below the level of the fourth interspace. The angle required to penetrate the body of the fifth lumbar vertebra and to enter the sacrum must then be decided, and a large drill is inserted through the body of the fifth lumbar vertebra obliquely, nearly directly downward, as the patient lies supine. Its point can be felt passing through the lower or posterior border of the body of the fifth lumbar vertebra, to enter the intervertebral space and then pass on into the new resistance of the sacrum. The depth of the hole made by the drill and the length of graft required may be predetermined by measurement. A bony transplant from the tibia or any other source, of the same diameter as the hole, is then tamped gently into place; the subperitoneal tissue is approximated with interrupted catgut and the posterior peritoneum with a running stitch of catgut, and the abdomen is closed completely without drainage.

No plaster bed or splint seems necessary in after-treatment. A moderately firm mattress or fracture bed, which permits nursing care without flexion of the back, is used. Confinement in bed lasts eight weeks and is followed by ambulation and the use of a steel back brace until there is roentgenologic evidence of bony fusion.

REPORT OF A CASE

My investigation brings to light the first instance of anterior fusion of the bone, done by Jenkins, the second, by Burns, the third, by Mercer using Burns's method (his patient died two years later in childbirth) and the fourth and fifth, by Mercer using his own technic. In the fourth instance, the patient died on the eighth postoperative day, after passing blood in the stools; postmortem examination showed thrombosis of the superior mesenteric artery. The patient in the fifth instance was well one year after operation. The sixth instance was in a case of mine, in which the operation was performed without knowledge of any of the others except the first.

B. P., a man aged 48, was admitted to the Presbyterian Hospital at Chicago on April 26, 1937. In 1922, when he was working in the tallow and hide business, a wagon he was driving turned over, and he jumped to avoid injury. One foot was caught by the toe so that in jumping and falling he twisted his back. He had severe pain in the lumbosacral region but was able to get up, rehitch his team and get back to quarters. A disabling back ache continued for several days, followed by apparently complete recovery from all symptoms. About three weeks after the accident he had progressive lameness in the left leg and later, while plowing, would stumble and fall. The claudication in the left leg persisted,

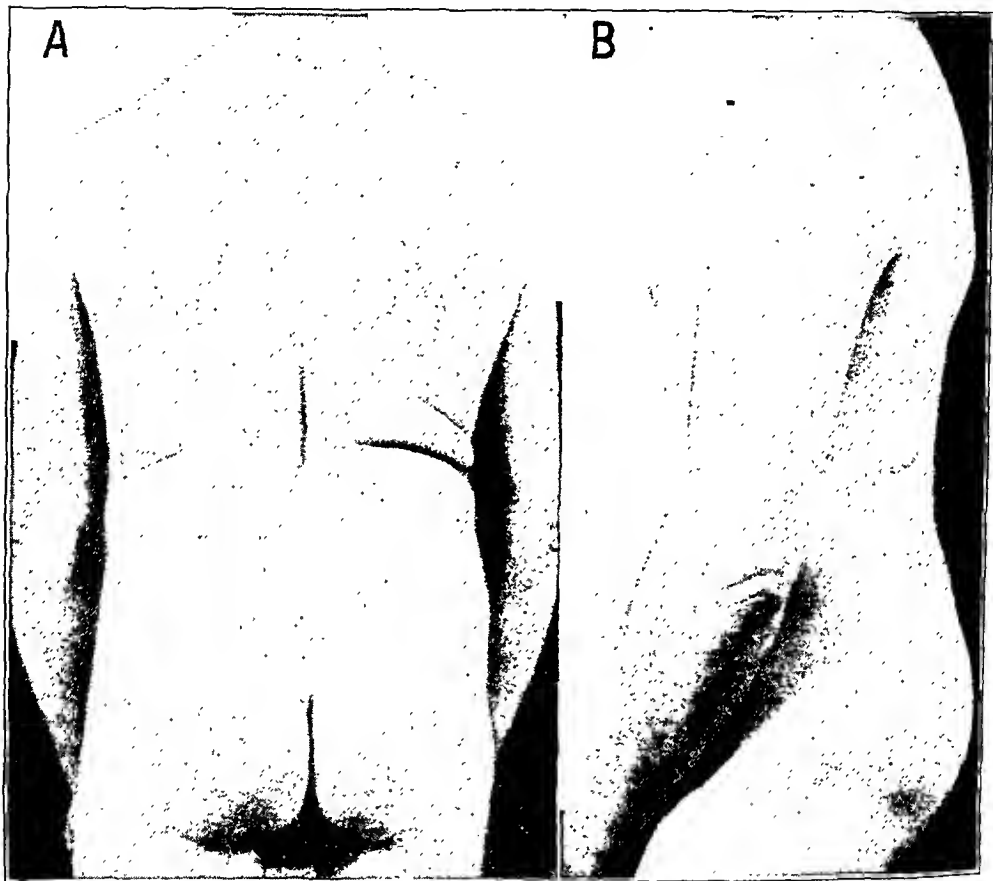


Fig. 1.—*A*, a man with spondylolisthesis viewed from behind. The depression at the lumbosacral level and the hypertrophy of the spinal muscles can be seen. The deep crease around and above the iliac crests is characteristic. *B*, lateral view of the same patient. The thoracolumbar lordosis and the protuberant abdomen are apparent.

but he continued at work, though complaining of continual back ache, until eighteen months before his admission to the hospital, at which time his symptoms became so aggravated that he had to cease work. In the five months preceding his admission he had become nervously irritable, and had had a small urinary stream, and his visual acuity had diminished.

Since the onset of his trouble he had been examined by several physicians, including irregular practitioners, and been subjected to numerous blood tests, all of which gave normal findings. Repeated roentgenologic examinations had demonstrated a slipping forward of the body of the fifth lumbar vertebra. Eighteen months before admission he fell down some stairs, after which accident the symptoms in his back and leg had increased in severity. A stricture was present, following a specific urethritis contracted more than fourteen years before, for which he was treated for two years by urethral injections. Urethral dilatation with sounds had been performed for the preceding three years with considerable benefit. All his teeth were extracted three years previously; he had undergone no major surgical operations.

The examination on admission showed a rather slender white man, 48 years old, not acutely ill, complaining of back ache with claudication in the left leg. The general physical and laboratory examinations showed little abnormality; there

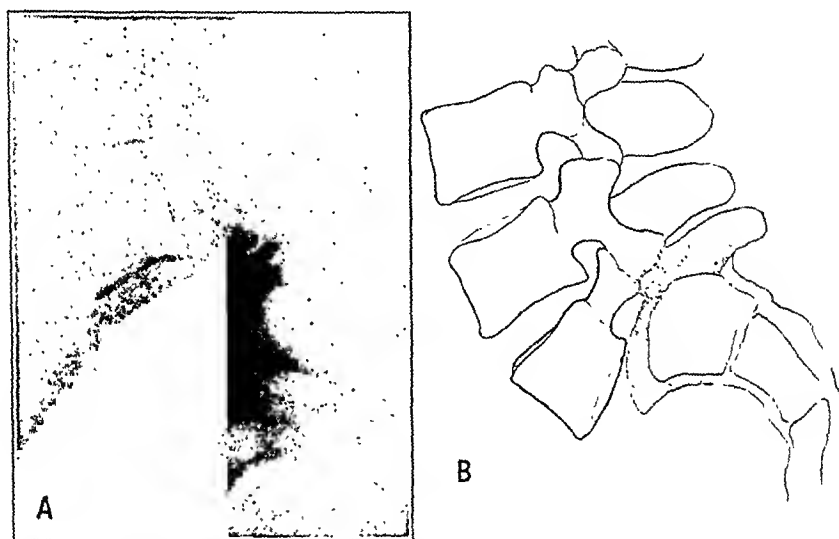


Fig. 2.—*A*, lateral view of the lumbosacral spine of the patient shown in fig. 1. The tipped axis of the sacrum and the projection forward of the body of the fifth lumbar vertebra with all the superimposed vertebral bodies are shown. The print does not show clearly the deficiency in the laminae. *B*, tracing of the roentgenogram. There is much new bone along the anterior and superior border of the base of the sacrum. The positions of the centrum and of the spine of the fifth lumbar vertebra are typical of spondylolisthesis.

were leukocytes in the urinary sediment, varying in amount on several occasions and accompanied by a trace of albumin when a high count was obtained. No casts were present in the urine. The patient's back was markedly lordotic, with a concavity at the lumbosacral junction, bounded on each side by outstanding and apparently hypertrophied spinal muscles. A finger placed in this cavity could palpate a bony floor, apparently part of the upper border of the sacrum. Extending from the depression was a bilateral transverse crease in the skin, extending as far as the posterior axillary line. The abdomen was protuberant but presented no hernias, no free fluid and no palpable masses. The prostate was moderately enlarged, smooth and firm and not tender. No arteriosclerosis was palpable, and

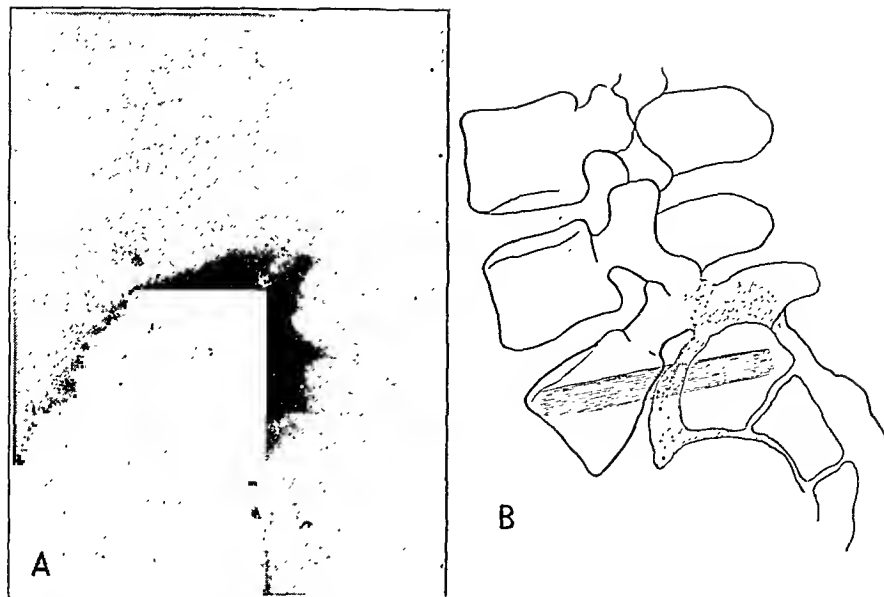


Fig. 3.—*A*, postoperative lateral view of the lumbosacral region. The transplanted bone penetrates through the corpus of the fifth lumbar vertebra, past the lumbosacral intervertebral space, on into the sacrum and nearly to the sacral canal. This transplant is sizable and should lead to bony fusion. *B*, tracing of the roentgenogram. No part of the transplant projects beyond the anterior margin of the body of the fifth lumbar vertebra.

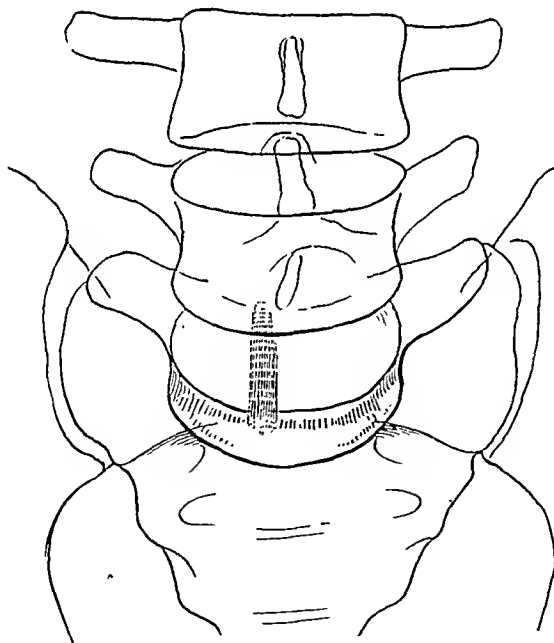


Fig. 4.—Tracing of a roentgenogram showing an anteroposterior view of the transplanted bone postoperatively. The transplant (or Smith-Petersen nail if used) appears foreshortened on account of its tilted axis. By intention the transplant is placed slightly to the right of the middle line, as this insertion avoids the arch of the iliac veins and vena cava as well as the middle sacral structures.

all tendon reflexes were normal except the patellar, which were slightly exaggerated. The count showed: blood hemoglobin, 95 per cent; erythrocyte count, 4,900,000; leukocyte count, 9,000, and polymorphonuclears, 72 per cent. The blood pressure was 140 systolic and 80 diastolic. The roentgenologic findings indicated a marked forward displacement of the fifth lumbar body on the sacrum, producing a sharp S-shaped curve at the lumbosacral junction and a thickening of the anterior margin of the first sacral segment. It was believed that there was a separation of the isthmus on both sides of the neural arch of the fifth lumbar

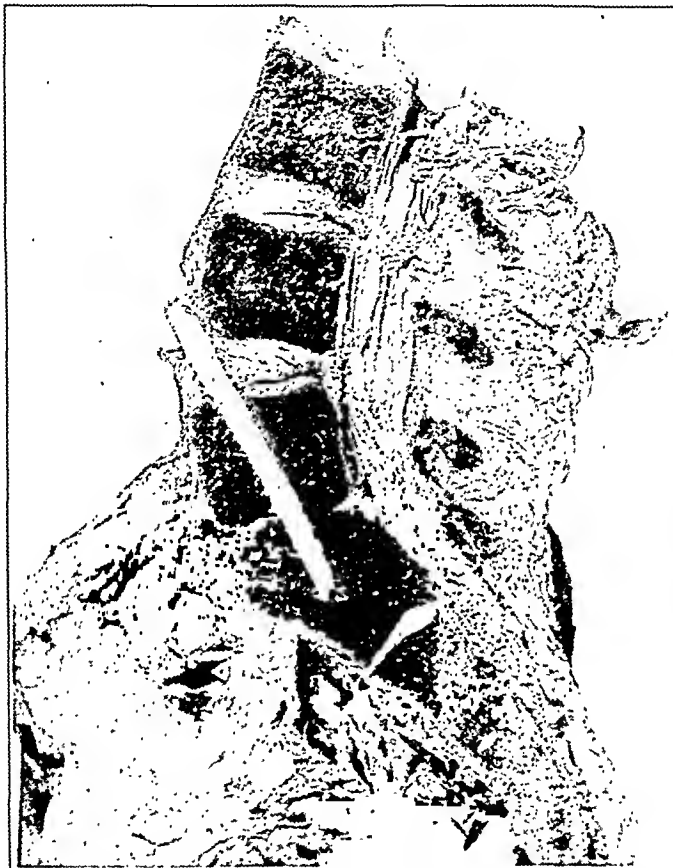


Fig. 5.—Section through a human (normal) pelvis after the insertion of a bony transplant for illustration. When spondylolisthesis is present it is not so difficult to insert the transplant or a Smith-Petersen nail as it is in the normal bone. The overhang of the body of the fifth lumbar vertebra permits a more direct and less oblique angle of insertion and a deeper penetration into the first sacral body.

vertebra, but this condition was somewhat obscured by cloudiness and by a small amount of new bone which blocked the view. In the posteroanterior view the centrum of the fifth lumbar vertebra cast a semilunar shadow, seen through the body of the first sacral segment. There was little scoliosis.

One day after admission, the patient was placed on a modified Rogers bed with skin traction on both legs and a jury-mast on the head for countertraction.

The amount of traction and the angle of the bed, extending the spine, were increased frequently up to the patient's limit of tolerance, until there was at least 40 pounds' (18 Kg.) traction on the legs. There was no apparent change in the deformity of the back, and a second roentgenologic examination showed no reduction of the displaced vertebra after ten days' trial of this method. After this attempt at reduction the patient was released from hyperextension of the spine, with traction, and prepared for operation, which was performed on May 10. He was placed under anesthesia induced with ethylene and a small amount of ether, and a transplant of his own bone was removed by the motor saw set at a width of $\frac{5}{12}$ inch (1 cm.) from the anterolateral surface of the right tibia, the wound being immediately closed and dressed.

The abdomen was then opened by a paramedian incision on the right, encircling the umbilicus and extending nearly to the pubis. Neither adhesions nor abnor-

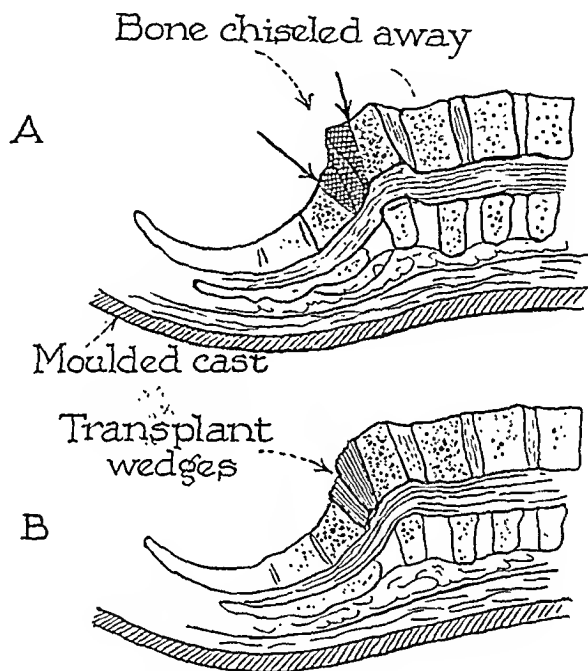


Fig. 6.—*A*, Mercer's operation, schematically drawn. The chisel cuts away the shaded area, removing the intervertebral disk and tissues with some bony surface. His description of the operation includes the fact that the patient lies on a previously prepared plaster of paris shell, so that no flexion or angulation of the spine is possible postoperatively. *B*, bone transplants wedged into the defect according to Mercer's description. He apparently intends transplants to hold by surface friction; hence the great care needed in handling the patient after the operation. Flexion at the lumbosacral junction might easily displace the wedges of transplanted bone.

malities presented themselves in the abdomen. The abdominal viscera were completely packed away from the sacral promontory by moist sponges. The patient's head was depressed about 20 degrees from the horizontal, and it was then possible to visualize and palpate the projecting body of the fifth lumbar vertebra where it overhung the upper sacral surface. A vertical incision was made through the peritoneum and the subperitoneal fat over the body of the

fifth lumbar vertebra and the fourth intervertebral space, slightly to the right of the middle sacral artery, which could be plainly seen. No special efforts were required to retract the aortic arch or left common iliac vein and inferior vena cava out of the field. (In some of the reported cases and in my study of the normal cadaver, it has been found necessary to apply a padded, flat retractor under the left common iliac vein or aortic bifurcation and also to tie an ascending vein which passes up the anterior surface near the middle of the sacrum to enter into either the left common iliac or the vena cava at the junction.)

The sympathetic nerve plexuses in this region were avoided by reflecting the peritoneum with its underlying fat and clinging closely to the bony surface with a small periosteotome. The anterior surface of the body of the fifth and the fourth interspace, easily recognizable, was adequately exposed, and a $\frac{5}{16}$ inch (1 cm.) drill was then inserted at the upper border of the fifth lumbar body and directed downward into the first sacral segment. The change in the resistance to the drill as it passed through the lower border of the fifth lumbar body into the lumbosacral interspace, traversed it and entered into the bony tissue of the upper sacral surface could be plainly felt by my hands operating the instrument. When sufficient penetration was obtained, the drill was withdrawn, and the tibial transplant was found to fit snugly enough to require but a slight amount of tamping to engage in the opening made by the drill and be sunk to a level which would permit closure over it. The subperitoneal fat was closed with a few interrupted catgut sutures and the peritoneum over that with a running catgut stitch. There was no oozing. The abdomen was closed in layers, and the patient was carefully lifted from the table and placed in an ordinary hospital bed without flexion of the spine.

His recovery was almost uneventful. On the third postoperative day his temperature touched 100.2 F. Both abdominal and tibial wounds healed kindly. On the second day he vomited a few times, never more than 75 cc. of material. He had trouble in urination, and a self-retaining catheter was with some difficulty inserted past his stricture. This was left in place two days and then withdrawn. On May 16 and 17 he had an involuntary urination, and on the night of May 16, harboring hallucinations, he got up out of bed! On May 25 he was placed on a Goldthwaite frame and a circular torso plaster of paris dressing was applied, holding the spine in slight extension. On June 17 he was discharged, wearing this plaster corset. He made no complaint of pain in the back; his old distress was gone; he had no difficulty in urination or control of his bowels, and the wound was healed. He was fitted with a side iron to protect the right tibia, from which transplant had been removed, against injury. He left using crutches on account of the heavy plaster and long confinement in bed with subsequent loss of muscular strength. On August 17 the plaster corset was removed and a roentgenogram of the spine made. This showed the transplant in the same position in which it was placed. There was an area of lighter density about it, probably representing extravasated blood and some absorption of bone (fig. 3). The patient was reexamined on September 6. He was able to walk without support and had absolutely no pain in his back. There was still a little of the old dragging in the leg and tire in the upper part of the thighs after he had walked two blocks.

CARCINOMA OF THE BREAST

REVIEW OF FOUR HUNDRED AND THIRTY-NINE CASES

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ETIOLOGY AND SUSCEPTIBILITY

The cause of mammary cancer, in common with that of other types of malignant tumor, is not definitely known. Even though many facts have been learned, mammary cancer appears to have reached a point beyond which effective prevention seems well nigh impossible.

Chronic mastitis is believed by most authorities to be the principal predisposing condition, but cancer so often occurs without pronounced chronic mastitis or in a very early stage of mastitis that this theory in itself is inadequate to explain the frequent incidence. All will agree, however, that mammary cancer must be preceded by involutional or inflammatory changes. The sweat glands of the breast are frequently the site of origin, and the causation of lesions so originating is probably somewhat different from that of the common duct cancer. Cancer originating in the sweat glands usually appears near the skin and in the axilla and is particularly prevalent among persons with the seboreic diathesis.

Many observers have pointed out the prominence of stagnation of secretion in the cancerous breast, and Keynes (quoted by Ewing¹) has emphasized the part played by stagnation in chronic mastitis. Cheatele (quoted by the same author) also has emphasized the importance of chronic irritation by retained secretion in the development of cysts and periductal fibrosis complicating chronic mastitis.

The entire question has been greatly illuminated by Bagg,² who in a race of mice known to have a low incidence of cancer succeeded in producing mammary carcinoma in 85 per cent of cases merely by with-

From the Guthrie Clinic.

Thesis submitted to the Faculty of Surgery of the Graduate School of Medicine of the University of Pennsylvania in partial fulfilment of the requirements for the degree of Master of Medical Science (M.Sc. [Med.]) for Graduate Work in Surgery.

1. Ewing, J.: The Prevention of Cancer, Surg., Gynec. & Obst. **44**:165, 1927.

2. Bagg, H. J.: The Functional Activity of the Breast in Relation to Mammary Carcinoma in Mice, Proc. Soc. Exper. Biol. & Med. **22**:419, 1925.

drawal of the suckling young immediately after birth, thus allowing stagnation to occur in the breasts of the female mouse. Adair³ reported that in only 8 per cent of 200 cases of mammary cancer was there a history of normal lactation. In following his work further he found that a great many of the patients showed large amounts of inspissated or puriform material, which could be withdrawn by means of the breast pump. A similar phenomenon was noted with chronic mastitis, and after removal of the retained material the indurated nodules and cysts often completely disappeared.

There exist, then, clinical, anatomic and experimental data indicating that stagnation of secretions is a prime factor in the causation of chronic mastitis and of mammary cancer, and a basis is thus laid for the hygiene of the breast and for the prevention of mammary cancer.

One of the few known facts about cancer is its relation to age. In women the senile changes taking place during the fourth and fifth decades are definite factors in bringing about cellular changes which invite cancer. W. J. Mayo⁴ made the statement that cancer does not appear in sound tissue and that the one provocative agent which remains unchallenged is chronic irritation. In all lands and among all peoples we see this one causative influence in the ascendant. Carcinoma of the scalp is particularly common among those Chinese who shave their heads with a dull and rough-edged razor, but it does not appear in those who do not follow this custom. The eating of hot rice by the men, who eat at the first table, is frequently the forerunner of carcinoma of the pharynx and of the esophagus. The condition does not appear in the women, who eat at the second table, when the rice is cold. In Australia, the sharp-edged sand blown by hot winds in the desert section of the country so frequently produces cancer of the face that such cancer is called the Australian disease. In certain parts of India and the Philipines, where betel nut and lime are still chewed, cancer of the buccal mucous membranes is common. Many instances of chronic inflammation produced by tobacco, by hot pipe stems and by ragged stumps of teeth can be cited, showing such inflammation to be definite predisposing factor in the production of cancer. In countries where the breasts are allowed to be exposed, that is, are not compressed or irritated by covering, carcinoma is rare. Cancer of the breast occurs chiefly among civilized women. In the mountain regions of Kashmir, India, where the people carry braziers filled with hot coals strapped on the lower part of the abdomen, cancer just above the pubis is common. A possible explanation is that when the tissues have been subjected to a

3. Adair, F. E., and Bagg, H. J.: Breast Stasis as the Cause of Mammary Cancer, *Internat. Clin.* 4:19, 1925.

4. Mayo, W. J.: Susceptibility to Cancer, *Ann. Surg.* 93:16, 1931.

long-continued insult the reparative processes are exhausted; instead of healthy cells, less mature cells are thrown into the breach of continuity; finally, embryonic cells replace the normal cellular structure.

Newer revelations seems to indicate that cancer may be the result of agencies acting from within the body (as well as from without) due to biochemical dysfunction affecting the life history of embryonic cells. Whatever the nature of the agencies producing malignant tumors, it is evident that they are inseparable constituents of the cell, as metastasis takes place only by the transplantation of the malignant cell itself.

In the final analysis, cancer is a recessive condition. Roughly, about 10 per cent of all persons have cancer in some form, while about 90 per cent escape. It is not logical to assume that persons in the latter group do not come in contact with some or all of the causative factors. It would seem that susceptibility to the causes of malignant degeneration, whatever they may be, is subject to individual variation and that increasing age tends to lessen the reparative powers and to decrease immunity. The work of Maud Slye in breeding strains of mice, which is familiar to all physicians, bears out this contention and shows very well the importance of heredity in resistance or susceptibility to cancer.

AGE AND SEX INCIDENCE

Carcinoma is especially prevalent in the fourth and fifth decades, more than 50 per cent of all carcinomas being discovered during these years. Stubenbord ⁵ showed the following data:

Age at Onset, Years	Percentage
20-30	3
30-40	18
40-50	30
50-60	30
60-70	19

In Schreiner and Stenstrom's ⁶ series of 563 cases, 58 per cent of the lesions occurred between the ages of 40 and 60, while the statistics of Moschcowitz and Colp ⁷ (218 cases) and those of Judd ⁸ (651 cases)

5. Stubenbord, J. G.: Cancer of the Breast, Surg., Gynec. & Obst. **52**:1001, 1931.

6. Schreiner, B. F., and Stenstrom, A. T.: End Results in Five Hundred and Sixty-Three Cases of Breast Cancer, Surg., Gynec. & Obst. **44**:609, 1927.

7. Moschcowitz, A. V., and Colp, R.: Late Results After Amputation of the Breast for Cancer, Ann. Surg. **84**:177, 1926.

8. Judd, E. S., and Sistrunk, W. E.: End Results in Operation for Cancer of the Breast, Surg., Gynec. & Obst. **18**:290, 1914.

showed the occurrence of 51 and 43 per cent, respectively, between these ages.

Table 1 shows the age incidence of cancer of the breast in various series.

Although various methods of defining the age decades are used, such as from 21 to 30 or from 20 to 29, and although in some series the age at operation rather than the age at onset is used, the data given in the table are accurate for all practical purposes. It is plainly seen that the maximum incidence of cancer of the breast occurs between the ages of 40 and 50 years. In this connection, it is said that in Switzerland the peak is reached from two to three years later than in the neighboring German-speaking countries.

Carcinoma occurring in persons under the age of 20 is rare and usually is reported in the literature. There was only 1 such lesion in

TABLE 1.—*Age Incidence of Mammary Cancer*

Author	No. of Series	Under 20	20-29	30-40	40-50	50-60	60-70	70-80	80-90
Schreiner and Stenstrom ⁶ ..	363	0	6	49	150	152	112	50	13
Pfahler, G. E., and Widmann, P. P.: <i>Am. J. Roentgenol.</i> 14:559, 1925	801	2	20	79	285	243	122	43	2
Harrington ⁹	2,083	1	31	394	732	611	303	94	5
Guthrie ¹⁰	453	0	7	23	99	86	68	30	2

Harrington's ⁹ series and none in the Guthrie Clinic ¹⁰ series. In this series, 4 carcinomas, or a little less than 1 per cent, occurred in male patients. Three of these male patients are dead of cancer after two years, and 1 is alive, with recurring cancer.

Winslow ¹¹ had 3 male patients in 102 cases. He also reported a case in which a fibroadenoma occurred in the breast of a 17 year old girl. This tumor was malignant at the time of its removal.

As far as racial incidence is concerned, it is interesting to note that, according to Stubenbord,⁵ cancer of the breast occurs infrequently in members of the Negro race. He reported only 2 instances in 108 cases in which the patients were of fourteen different nationalities. Because of the diffuse admixture of races in the Guthrie Clinic series it was impossible to arrive at any conclusions concerning racial distribution.

9. Harrington, S. W.: *Carcinoma of the Breast: Surgical Treatment and Results*, J. A. M. A. 92:208 (Jan. 19) 1929.

10. Guthrie, D.: *The Rodman Operation for Breast Cancer*, J. A. M. A. 63:1256 (Oct. 10) 1914.

11. Winslow, R.: *An Analysis of One Hundred and Two Cases of Tumors of the Breast*, Ann. Surg. 74:341, 1924.

RELATION OF CARCINOMA TO CHRONIC CYSTIC MASTITIS

Much has been written in regard to chronic cystic mastitis and its relationship to cancer of the breast. Bloodgood¹² repeatedly has presented careful histologic studies of the various benign tumors of the breast, with comments on their etiologic relationship to cancer. He concluded that cancer does not often develop in a breast presenting a single large cyst but is frequently associated with the diffuse type of the disease. This opinion seems to have been shared by most writers.

The role of stasis and faulty drainage of the breast has received much attention in this respect. Adair and Bagg,³ whose work with mice has been referred to, concluded that stasis is significant in giving rise to proliferative changes and subsequently to cancer.

Campbell,¹³ in a complete review and analysis of the literature, stated that the histologic evidence in favor of the theory that cystic disease is precancerous may be summed up as follows:

1. Cystic disease is frequently found in association with frank carcinoma.
2. Various gradations of epithelial proliferation may exist to give the impression that cystic disease represents a progressive evolution of epithelial hyperplasia eventuating in carcinoma.
3. The examination of tissue removed from breasts containing cystic disease frequently reveals histologic pictures which may be interpreted as representing early cancer.

He went on to say, however, that cystic disease is not a precancerous lesion and that malignant changes are no more likely to develop in a breast showing the disease than in one which is entirely normal. He presented the following review of Bloodgood's work in this connection:

An entirely new approach to the problem is offered by Bloodgood. Convinced that most cases of cystic disease never become malignant and that many needless amputations were being done, he practiced limited operations and followed his patients for years to determine the incidence of carcinoma. Thus he obtained a correlation between the various histologic pictures and the clinical course of the disease.

It is of interest that in 1904 Bloodgood, basing his opinion on microscopic criteria only, had concluded that malignant epithelial change occurred in 10 per cent of all cases of cystic disease. In 1906 he wrote that adenocarcinoma was already present in over 50 per cent of patients with the adenocystic variety of the disease whom he had examined.

In 1921, having changed his opinion, he reported his experience with 350 cases of cystic disease, in 128 of which the treatment had been local excision only. A follow-up showed that carcinoma had developed in 3 of these cases, an incidence

12. Bloodgood, J. C.: *Borderline Breast Tumors*, J. A. M. A. **104**:439 (Feb. 9) 1935.

13. Campbell, O. J.: *Relationship Between Cystic Disease of the Breast and Carcinoma*, Arch. Surg. **28**:1001 (June) 1934.

of about 2 per cent. He concluded that with the exception of nonencapsulated cystadenoma, or, as it is here termed adenocystic disease grade II, cystic disease is not a precancerous lesion and cancer is no more likely to develop in a breast so involved than in a normal one.

In 1929 he amended this impression by including diffuse nonencapsulated cystadenoma among the benign lesions. He had recognized this variety of the disease in over 100 patients and treated them without operation. Malignant tumors did not develop in any of them. In the same year he reported his experience with over 300 cases in which blue domed cyst was treated by local excision. A follow-up over a period of years showed no greater incidence of carcinoma than in women with normal breasts.

Reviewing his locally removed "border-line" tumors in 1931, he found that all of these patients, over whose diagnosis pathologists had disagreed fifteen years before, were living and well or had died of other causes without having shown evidence of cancer.

Bloodgood has therefore concluded from his years of study, combining and correlating microscopic pictures with the clinical course of the disease, that cystic disease *per se* is not a precancerous lesion.

Campbell¹² did not advise the amputation of breasts with cystic disease because of the risk of malignant degeneration. He stated that the conservative policy toward cystic disease of the breast "is based on the fear that carcinoma may be present and unsuspected at the time of the examination rather than on the fear that a malignant condition will subsequently develop." He concluded that cystic disease calls for an exploratory incision and frequently for a limited operation, but only rarely for amputation.

Campbell¹² also stated that all single solid tumors in women over the age of 25 should be removed for diagnosis. Gross diagnosis is possible in about 80 to 90 per cent of cases, but in a certain number microscopic examination of a frozen section must be resorted to. For single small localized areas biopsy is the safest method. In the presence of multiple tumors in one or both breasts, which is in itself strong evidence of the benignity of the process, it is advisable to remove one or two of the most questionable ones for examination, because if carcinoma is developing in a breast containing benign tumors it can be recognized clinically only after the characteristic late signs of malignancy have appeared.

Cysts large enough to be recognized clinically are usually benign. However, a malignant condition may be present in the wall of a cyst,¹³ and for this reason single cysts should be excised. The breast with the diffuse form of the disease, the shotty or nodular breast, need not be operated on but should be closely observed. When one area in a diffuse process stands out from the rest or seems to be developing at a more rapid rate it should be excised and examined. The remainder of the breast is of no aid in arriving at a diagnosis.

Bleeding from the nipple demands excision of the localized area of breast tissue for examination. Over 50 per cent of lesions in such cases will be found benign.¹³ If the sources are multiple, amputation should be resorted to, because only serial section can rule out a malignant lesion, and obviously this is not practical. If a malignant lesion is found, radical operation, of course, is to be performed. The same holds true when the pathologists is in doubt as to the true histologic picture.

MARITAL INCIDENCE; PREGNANCY AND LACTATION

Stubenbord⁵ found that 81 per cent of carcinomas of the breast occur in married women and 10 per cent in unmarried women, while Schreiner and Stenstrom⁶ reported 85 per cent in married women and 15 per cent in single women. Roughly, 83 per cent of patients in the series here reported were married and 17 per cent were unmarried. Possibly lactation, pregnancy and trauma of feeding play a part in the production of malignant tumors, although Burton J. Lee¹⁴ concluded otherwise. Physicians have been taught that cancer of the breast occurs more frequently in women who have had previous lactation, but Lee¹⁴ believed this to be an incorrect assumption and said that, although the larger number of patients will be found to have had previous lactation, the percentage of this group in the total population of women over 25 years of age is probably much higher than that of women who have never lactated. No absolute proof of a higher incidence of mammary cancer in the latter group has been found.

In 315 cases in which data on the marital incidence were available, 28.2 per cent of the patients had never been pregnant, and of the 71.8 per cent that had been pregnant 90.7 per cent had breast-fed their children. The average number of children in 396 pregnancies was 1.8. The average age at onset of symptoms when the patient had breast fed the children was 45.4 years, as contrasted with 44.1 years when the children had been bottle fed. The average age at onset of symptoms when the patient had never been pregnant was 46.2 years.

These figures showing the average age of incidence are of some interest. They indicate that carcinoma develops somewhat earlier in the breast which has not met the physiologic demands incident to pregnancy and appears latest in those which did not suffer the physiologic changes of pregnancy and the possible trauma incident to breast feeding. In the same group of cases only 1 carcinoma arose within three years of pregnancy; the patient was a 34 year old woman who first noticed the mass in the breast twenty-eight months after nursing her first child. She

14. Lee, B. J.: End Results in the Treatment of Cancer of the Breast by Radical Surgery Combined with Preoperative and Postoperative Irradiation, *Tr. South. S. A.* 45:201, 1933.

had had lumps in the breast before, but they had disappeared previous to her pregnancy.

Bloodgood¹⁵ discussed the microscopic picture of encapsulated tumors removed from the breast during pregnancy or lactation, and in no instance was he able to find in these adenomas anything that resembled the microscopic picture of cancer.

GROSS PATHOLOGIC DIAGNOSIS

The gross diagnosis of mammary cancer is of increasing importance at the present time, chiefly because of the fact that patients are becoming educated to the significance of any tumor in the breast and are, therefore, presenting themselves earlier for medical examination. Cancer can be cured, but only as a result of early diagnosis and early appropriate treatment. Concomitantly, an increasing number of borderline cases is observed, in which the clinical diagnosis is doubtful. Frequently there is no question as to the diagnosis of mammary cancer immediately before an operation, because there are, unfortunately, many patients who have been suffering from cancer for months or years and have sought the advice of a physician only at the repeated urging of relatives or because that all-too-late danger signal, pain, has appeared. In such patients, with a large, hard, possibly ulcerated mass with extensive metastases to the axilla, the neck and the chest, there is little difficulty in diagnosis from a clinical point of view. Operative or postoperative pathologic diagnosis is of little value except in determining the degree of malignancy and the probable duration of life.

The diagnosis of early mammary cancer presents difficulties, yet the diagnosis must be made if the patient is to be cured. The surgeon and the pathologist alike must be familiar with the gross appearance of malignant tumors in order that appropriate treatment may be afforded the patient. Whether or not the services of a pathologist are available at the time of the operation, the surgeon must be competent to recognize carcinoma when it is present. The operative procedure to be advised depends on his accurate observation. Such accuracy is obtained only by careful study of the gross specimen and by correlation of its evidence with the evidence offered by the frozen section. By the use of this method it will be possible in the vast majority of cases to make an accurate diagnosis by gross examination alone.

It is the accepted policy of most surgeons today to advise the removal of any questionable lump in the breast and to subject it to microscopic examination. However, many patients are advised to wait until the mass makes its presence known by pain or by some other symptom. Carcinoma in the early stages is painless, and by the time it manifests

15. Bloodgood, J. C.: Biopsy in Breast Lesions, *Ann. Surg.* **102**:239, 1935.

itself to the patient it is usually too late to do anything except provide palliative treatment. It should always be advised that if a nodule removed proves to be malignant radical amputation is the action to be followed. If facilities are not available for immediate microscopic examination and the tumor is believed clinically to be malignant, a radical amputation should be done and a pathologic report studied later. In a great majority of cases "a single, hard nodule, with restricted mobility in an otherwise normal breast, is usually cancer." Likewise "every single, solid painless lump in the breast at any age should be considered cancer until ruled out by microscopic section." There may be multiple carcinomatous nodules in the breast, because it is not uncommon for cancer to arise from cysts or in chronic mastitis. Palpation is a valuable procedure and is best done with the flat of the hand against the chest wall. The patient should be examined in the supine and sitting positions with the arms extended above the head. The common fibroadenoma is frequently but not always single and is rarely fixed, being freely movable in the breast tissue. A malignant nodule, on the other hand, is more or less firmly fixed to the skin, to the fat or to the wall of the chest, frequently with dimpling and retraction of the nipple. There are occasional exceptions, in which a malignant tumor may be freely movable; this happens when carcinoma is confined to a cystic capsule and has not yet penetrated to the surrounding tissue. Also, in occasional cases fixation to the skin, with dimpling and restricted mobility, is associated with the inflammatory reaction of a benign tumor.

The consistency of the more common tumors is of some aid in arriving at a diagnosis. Carcinoma has a hardness peculiar to itself, resembling the hardness of cartilage, and is almost angular at times. Adenoma is usually softer than carcinoma and even when hard feels more like a hard rubber ball, there being a sense of slight compression. Occasionally a cyst under great tension feels solid; this may confuse the diagnostician. An occasional carcinoma (particularly if it arises from a cyst) may feel moderately soft and if associated with a residual cyst formation will escape notice. Even extensive involvement of the breast by the organized tissue of chronic mastitis does not give the same impression of hardness as does cancer. The tissue of mastitis is more resilient and has a rubbery toughness, making it somewhat difficult to cut, but it never has the scarlike appearance or the cartilage-like texture of carcinoma.

The color and the transparency of a mammary tumor are of some value in showing the type of lesion present. Valuable information can be gained by looking at the cut surface; carcinoma may show yellowish or white streaks or points. These vary in size and number and represent fine ducts filled with proliferated cells undergoing fatty degeneration.

The points are cross sections, and the streaks are ducts cut longitudinally. Diffuse carcinoma in which there is no definite tumor may give trouble, but the points usually can be found. Many sections may be necessary.

Gelatinous or mucoid carcinoma may not show the opaque structure or the points, but thin translucent gelatinous material may infiltrate the breast. Traumatic fat necrosis (clinically much like carcinoma, and a form of lesion which will be mentioned later) fails to show these features in the gross. Of course, hemorrhage, infection or extensive necrosis will complicate the picture.

In a large tumor which has originated in a cyst and has filled it and become solid, the entire cut surface may be pale yellow or orange, with a grayish granular surface, from which cellular material (sometimes called "cancer milk") may be scraped with a knife. The benign adenoma has a white translucent surface, and no cellular debris can be scraped off. The dense tissue of mastitis is white and waxy, has no yellowish points or streaks and is acellular. Scraping it produces nothing. There are in addition widely scattered cysts of various sizes throughout the tissue.

In some patients the breast is the site of long-standing mastitis; the glandular tissue feels like a mass of knotty cords without an isolated tumor mass. Section in these cases frequently presents difficulty in reaching a dilated duct filled with a putty-like greenish to gray material. The tissue is vascular and edematous, and the gross appearance is alarming. The breast is diseased, but the malignant condition is frequently limited to the ducts, and infiltration is lacking. Microscopic examination is necessary. The condition is considered precancerous, and a simple rather than a radical operation is the rule. If the clinical evidence of a malignant condition is not conclusive, if the tumor is thought to be benign or if the diagnosis depends on microscopic examination of the tumor the whole tumor and not a piece should be removed, because the gross picture is helpful, and dissemination must be prevented.

CLINICAL DIAGNOSIS

The diagnosis of tumor of the breast is becoming increasingly difficult, because patients are coming to the physician earlier than ever before, showing lesions so small that signs of malignancy have not yet developed. This is especially true of women between the ages of 35 and 50. During these years cancer of the breast in the early stages is commonly confused with fibroadenoma, cyst, mastitis or fat necrosis, and each of these must be considered and ruled out. In general, there have been no new data on symptoms of cancer of the breast. The average preoperative duration of symptoms gives some indication of the

rate of growth and the degree of malignancy. Malignant tumors of the breast may be divided into two classifications: sarcoma and carcinoma. The diagnosis of the former is usually simple when the two main types are considered. The first of these is true sarcoma, which results from a preexisting fibroadenoma. There is usually a history of a tumor preexisting for many years, which suddenly begins to grow rapidly. The tumor assumes large proportions, invades the skin and proceeds to central necrosis. Softening and ulceration characterize a still later stage. The salient feature is a tumor of long standing which suddenly exhibits rapid growth and then breakdown. Neurogenic sarcoma is the second type and is probably equally common. This is not a true tumor of breast tissue but has its origin in the nerve sheath. It is round, firm and noninfiltrating. The treatment is wide mastectomy.

To treat adequately of the diagnosis of the second class of malignant tumors of the breast, carcinoma, one must distinguish the different types, because each has its own clinical characteristics and life history, and each has a different prognosis. The first, scirrhus carcinoma, or fibrocarcinoma, is a stony hard, irregular nodule, frequently attached to the skin and causing dimpling, retraction of the nipple and deformity of the breast. The tumor is slow growing and slow to metastasize, and because of these facts radical amputation offers a high percentage of cures.

The adenocarcinoma found in the breast is of a higher grade of malignancy than scirrhus carcinoma. The lesion is localized, but it does not have the drawn, scarlike appearance of the scirrhus cancer. Later in its development it breaks down and ulcerates. Metastases are late, but when they do occur they represent a serious advance in the progress of the disease. Radical surgical treatment produces good results when the growth is confined to the breast.

Duct carcinoma, or comedo carcinoma, represents a third type, which invades the entire breast but remains confined there until it is ready to permeate the confining tissues. Frequently there is only slight change in the contour of the breast, or none at all, and the growth may thus be overlooked. Retraction of the nipple, adherence to the skin and the typical pigskin appearance are later features of the picture. Here the prognosis is more serious than for the two preceding types of cancer, and wide excision of skin should be practiced.

Sweat gland carcinoma has as its characteristic feature its eccentric position in the periphery of the breast, usually in the mammary fold. Histologically it is a variety of adenocarcinoma and is easily diagnosed under the microscope because its cells take only the eosin stain. The lesion appears to be attached to the skin, moving with it, and is not so firmly fixed to the deeper tissues as is the adenocarcinoma. The axil-

lary glands are not involved so early in the course of the disease as in other types of carcinoma of the breast. The treatment is the same as that for adenocarcinoma.

Papillary cystadenocarcinoma is a type of malignant tumor which begins in one of the terminal ducts as a benign papilloma, most commonly situated in the ampulla, at the edge of the areola. It may remain benign for many years, but it continues to grow and later infiltrates the basement membrane and invades the surrounding tissues, becoming a true carcinoma. This variety is frequently responsible for a sero-sanguineous discharge from the nipple often lasting for years. The neoplasm is of a comparatively low grade of malignancy, but, like most mammary carcinomas, it offers a bad prognosis once the axilla becomes involved.

Gelatinous carcinoma is of low grade and is easily cured by radical excision, but if recurrence takes place the prognosis is bad because of the insistence of the growth. It is radioresistant, and the best hope of cure lies in radical and early excision.

The anaplastic type of carcinoma, the next under consideration, is a small growth, fairly hard, frequently mistaken for fibroadenoma and consequently many times wrongly diagnosed. The tumor is composed mostly of loose, rapidly growing, highly malignant cancer cells in a small amount of fibrous stroma. Metastases to bone are early and common even though the tumor is small in size. It is highly radiosensitive and should not be operated on until after a course of irradiation has been given. However, because of the difficulty in making an early and positive diagnosis, the treatment is usually not specific, and the mortality is high. Irradiation of both primary and secondary growths is of first consideration in the treatment, and excision should be done whenever possible.

Inflammatory carcinoma has a characteristic appearance. The involved skin of the breast has a sharply defined edge due to the invasion of the dermal lymph spaces by carcinoma cells. The picture resembles that of erysipelas. The lesion spreads rapidly through the skin. Irradiation is the treatment of choice; operation should not be attempted. The prognosis is essentially bad.

DIFFERENTIAL DIAGNOSIS

The diagnosis of fibroadenoma usually is not difficult. This is a round, smooth, firm tumor, not stony hard as is carcinoma. It is freely movable and has no cutaneous attachment. It is most frequently found in women under the age of 40, but even though the clinician feels strongly that the lesion is a benign one the safest procedure is to advise its removal and a detailed examination.

Cysts of the breast, unless they are of noticeable size, are difficult to diagnose. The small ones are tense and hard and may early be confused with fibroadenoma. They are not infrequently somewhat inflamed and hence attach themselves to the skin, simulating the clinical picture of a malignant tumor. If the presence of a cyst is strongly suspected, an aspiration needle may be introduced. This will clarify the diagnosis. The method of transillumination suggested by Cutler¹⁶ has been used in this clinic, with a certain degree of diagnostic accuracy.

The diagnosis of mastitis when the condition is localized is never certain. The disease occurs in the cancer-bearing age and is not so frequent after the age of 55. The lesion is firm and irregular, with round nodules of varying size over its surface. It lacks the characteristic feeling of infiltration found in carcinoma; however, it is not freely movable with the breast tissue. It does not become fixed to the chest wall. If the lesion is multiple the diagnosis is much simpler. Again, the affected parts should be removed and subjected to detailed examination to determine the diagnosis and to rule out the presence of a malignant tumor in an early stage.

Mastitis should be divided into four types to facilitate diagnosis:

1. Cystic mastitis and fibrous mastitis are readily diagnosed. It is commonly found that the masses in the breast are rounded, irregular and indefinite. The lesions are firm and multiple. Pain at the time of the menstrual period or immediately before it is a common complaint.

2. Tuberculosis of the breast (Lee and Floyd¹⁷) was not a proved clinical entity until 1881, when Dubar proved microscopically the presence of tuberculosis in breast tissue. It is not a common lesion and, according to Barker, occurs once to each 50 occurrences of mammary carcinoma. Only about 4 per cent of patients in whom this condition occurs are men. Like carcinoma, it usually occurs during the reproductive years; however, carcinoma tends to appear oftenest in the latter years of this period. Fifty-eight per cent of carcinomas in the cases reported by Lee and Lloyd¹⁷ were primary, no other focus being found.

The earliest symptom in 75 per cent of cases is a painless lump in the breast. A small percentage of patients have pain, and the rest show such symptoms as discharge from the nipple and sinus formation. The condition may resemble a malignant lesion, in that there may be retraction of the nipple and pigskin appearance of the surrounding skin. The mass may feel irregular, fixed and indurated and may show abscess formation. If the last-mentioned symptom is present together with

16. Cutler, M.: *Benign Lesions of the Female Breast Simulating Cancer*, J. A. M. A. **101**:1217 (Oct. 14) 1933.

17. Lee, W. E., and Floyd, W. R.: *Tuberculosis of the Breast*, Ann. Surg. **99**:753, 1934.

sinus formation, tuberculosis is to be strongly suspected. A serosanguineous discharge is an important confirmatory finding. There is involvement of the lymph glands in over 50 per cent of cases. Carcinoma with sinus formation may closely resemble tuberculosis, but this stage of carcinoma is becoming rare as the work of public education goes on. In many instances absolute diagnosis cannot be made in the gross and resort must be had to microscopic examination of the tissue.

3. Syphilitic mastitis, according to Thomas,¹⁸ occurs most commonly in women, only 25 per cent of patients in reported cases being men. Bilateral involvement is common. The tumors may be either single or multiple and may vary in size from a barely palpable nodule to a mass some 3 to 4 inches (7.6 to 10.1 cm.) in diameter. The tumors are hard, well circumscribed and movable. They may be subcutaneous or embedded within the parenchyma. The axillary glands are seldom involved. The tumors if untreated progress to ulceration and sloughing, with the punched-out appearance typical of ulcerating gummas. Pain is not a common finding and when present is not so severe as that of carcinoma. Carcinoma appears later in life than does gumma. A positive serologic reaction is of prime importance in the diagnosis.

4. Plasma cell mastitis, the last of the four types of mastitis, is a curious unexplained inflammatory process which tends to spontaneous regression and disappearance. It shows a rather characteristic history and has the general clinical signs of a malignant lesion. Usually, during the course of lactation the breast becomes acutely inflamed and presents a clinical picture simulating that of inflammatory carcinoma. A mass develops suddenly in the breast, and there is tenderness and redness of the skin. The entire breast becomes swollen, the axillary glands are enlarged and tender and there is occasionally a discharge from the nipple. The mass subsides partially but not completely, leaving a hard lump. The most important point of difference from inflammatory carcinoma is the absence of dermal thickening, representing invasion of the skin by malignant cells. There is attachment of the nipple and occasionally an orange-skin appearance to the epidermis. The acute symptoms soon subside, and the residual mass takes on many of the characteristics of a malignant tumor. In addition to these symptoms of cancer the mass itself shows hardness and a feeling of infiltration. The mass, however, very slowly decreases in size, and this is the crucial sign which enables it to be differentiated from carcinoma in this stage of the disease. Other important diagnostic aids in the differentiation of plasma cell mastitis from carcinoma are the acute onset of the disease and its subsequent clinical course.

18. Thompson, L.: Gumma of the Breast, *J. A. M. A.* **74**:791 (March 20) 1920.

Traumatic fat necrosis (described by Burton J. Lee¹⁴) is most common during the fourth and fifth decades, according to Cutler,¹⁶ and can easily be mistaken for a malignant tumor both in its appearance and in its clinical characteristics. Trauma is an essential etiologic factor, and although it is found with a history of carcinoma it occurs much more frequently in cases of fat necrosis. Hemorrhage into the fatty tissue, with resultant fibrosis, seems to be the pathologic process. Fat necrosis resembles carcinoma in many respects. At first, there is a rapid increase in the size of the mass, due to proliferation of connective tissue in response to the chronic inflammatory process. Proliferation may not be apparent until several weeks or months after the injury.

Adherence to the skin is a common feature, and retraction of the nipple may be present, leading one immediately to suspect malignant tumor. The consistency of fat necrosis is like that of carcinoma, and there may be fixation to the deeper underlying structures, although in most cases the tumor of fat necrosis is fairly well circumscribed and can be moved around in the breast tissue with greater ease than can a malignant tumor.

Radical excision, of course, is not necessary, fat necrosis being classed with the benign lesions of the breast.¹⁹

Paget's disease of the nipple is a condition which is said to be most common in women between the ages of 35 and 50. It first manifests itself as intractable eczema of the nipple. The area around the nipple is usually bright red and inflamed, with a finely granular surface. The surface may be moist and weeping, with a grayish exudate, or dry and scaly. The border is circinate and slightly raised. Within two years usually but occasionally not for as long as ten years, carcinoma appears in the breast. The debate as to which condition is primary seems still to be unsettled. There are those who follow Handley and believe that Paget's disease of the breast is essentially a malignant condition and that the eczema is the result of the carcinoma, while there are many others who follow Paget in believing that the disease begins in the skin, carcinoma of the breast being a secondary development.

19. In this connection, an interesting case has been recorded at the Guthrie Clinic since this paper was written. A woman, aged 60, was admitted with a history of trauma to the periphery of the upper middle quadrant of the right breast six weeks previous to admission. The injury was followed by painful swelling, which gradually subsided to a tender, ill defined mass. The mass was removed by simple amputation, and microscopic examination showed adenocarcinoma in the wall of a cyst, approximately 1 cm. in diameter, with a firm dry, whitish center. There were several areas of pigmentation, and evidence of old hemorrhage was present with the necrotic fat. There was no axillary involvement. Radical amputation was then done.

In any event, the recognition of Paget's disease calls for radical surgical intervention.

GROWTH AND SPREAD

Carcinomas of the breast showing involvement of the lymph nodes decidedly outnumber those that have no such involvement. In the cases reported by Moschcowitz and Colp,⁷ metastases to lymph nodes were present in 56 per cent, absent in 35 per cent and not mentioned in the report in 9 per cent. Stubenbord⁵ had 63 per cent, 28 per cent and 9 per cent, respectively. In this series of 439 cases, involvement of the lymph glands was present in 58 per cent, absent in 39 per cent and not mentioned in the report in 3 per cent. Thirty tumors were found to be inoperable through the primary axillary incision, and 17 of the patients died within one year of their examination. No trace of the others could be found.

TABLE 2.—*Involvement of the Axillary Lymph Nodes in Mammary Carcinoma*

Author	Nodes Not Involved, Patient Living and Well		Nodes Involved, Patient Living and Well	
	5 Years, Percentage	10 Years, Percentage	5 Years, Percentage	10 Years, Percentage
Harrington ⁹	63.6	44.1	24.3	13.4
Bunts, Frank E.: Ann. Surg. 70: 341, 1922....	35.0	18.0	20.0	8.8
White, W. C.: Ann. Surg. 86: 693, 1927.....	70.0	57.0	19.0	10.0
Guthrie ¹⁰	65.5	40.9	23.0	9.8

Gross evidence of axillary and cervical metastases was not present in all of the cases included, but microscopic examination revealed their presence, showing that metastatic carcinoma occurred much more frequently than nonmetastatic carcinoma. This may mean that involvement of the lymph glands occurs earlier than is suspected, but it more probably indicates in many cases neglect by the patient to attend to the smallest lump in the breast immediately on its discovery. In this connection the conclusions of Medical Report no. 34 of the British Ministry of Health²⁰ are interesting. They illustrate the extreme importance of undertaking the complete operation while the lesion is still confined to the breast and show that 90.1 per cent of patients in whom the lesion was thus limited were alive ten years after the operation, while 91.3 per cent of patients with axillary involvement were dead

20. The Late Results of Operation for Cancer of the Breast, Medical Report no. 34, British Ministry of Health, London, His Majesty's Stationery Office, 1926; cited in At the Heart of the Cancer Problem, editorial, Am. J. Surg. 27:187, 1935.

within ten years after the operation. Of patients having advanced carcinoma, 94.4 per cent were dead within ten years.

Education, of course, is the most potent weapon available to physicians in dealing with this phase of the disease. In the words of Sir George Newman: "Not 25 per cent of women with cancer of the breast obtain surgical treatment before their disease has gotten beyond the first stages." He said: "It is not because the disease advances rapidly. . . . The prime need in reducing mortality . . . is not extended hospital accommodations, not improved methods of treatment nor even diagnosis . . . it is avoidance of delay." The essence of the situation is to make sure that cancer of the breast is recognized immediately and is immediately treated.

To teach the laity the significance and the potential danger of a tumor in the breast would mean, in many cases, an earlier visit to the physician. To be sure, many more cases of almost certainly benign tumor would be seen, but in the presence of that word "almost" lies danger. To make certain the presence or absence of danger the tumor must be removed and examined by a competent pathologist. The patient should be told the possibilities of the diagnosis, and permission should always be obtained for a radical operation in the event that a malignant lesion is found. Using this approach of complete frankness, one seldom encounters a patient who will not cooperate in every way.

Routine roentgen examination of the chest and the pelvis should be done in cases of carcinoma of the breast, because of the large percentage of metastases to these areas. Lenz and Freid²¹ reported that in nearly 50 per cent (81 cases in a series of 168) of their cases such skeletal metastases were present, and Schreiner and Stenstrom⁶ reported that in 45 per cent of their cases metastases occurred in the chest, the spine and the long bones.

OPERABILITY

The simplest definition of operability from the clinical standpoint is that advocated by Lee,¹⁴ who stated that a tumor of the breast is operable when it is not fixed to the wall of the chest, whether or not the axillary lymph nodes have been invaded. In an inoperable cancer one or more of the following factors are present: Fixation of the tumor itself to the wall of the chest (with fixed axillary nodes); involvement of the supraclavicular or of the opposite axillary nodes; metastases to the chest or to bones; diffuse subcutaneous nodes; diffuse inflam-

21. Lenz, M., and Freid, J. B.: Metastases of the Skeleton, Brain and Spinal Cord from Cancer of the Breast and the Effect of Radiotherapy, *Ann. Surg.* 93:279, 1931.

matory cancer involving a wide cutaneous area; remote metastases. In such cases radical amputation should be withheld for two reasons. First, radical surgical operation on a debilitated patient shortens the life of the patient, and, second, it may bring discredit to surgery in the minds of the people. Cases must be chosen in which the tumor is really "operable." This in no wise indicates an unwillingness to perform palliative operations when they are indicated. The patient or, better, the relatives should be impressed with the fact that medical attention has been sought too late and that had the cancer been seen in its earlier stages it would probably have been amenable to surgical treatment. In 7 per cent of cases in this series the tumor was inoperable.

OPERATIVE TREATMENT

The modern conception of the radical operation for cancer of the breast derives from Halstead and from Willy Meyer. The evolution of the operation was well described by Rodman and its technic by Harrington.⁹ Unfortunately, the necessity for this radical operation is not universally appreciated, and various less radical procedures are still widely practiced, always with poorer results and fewer cures. In the less radical procedures the attempt is usually made to preserve the pectoralis minor muscle, and in many of them too much skin is preserved over the breast. Handley demonstrated the presence of invasion of the pectoralis muscle (Guthrie¹⁰) and the necessity for its removal.

Little of note has been added to knowledge in recent years of the requirements of technic in operations for cancer of the breast. Rodman (Guthrie¹⁰) in 1908 described an operation which embodies the essential principles required for the thorough surgical removal of a breast with a malignant tumor. There are two main principles: First, the operation must be complete enough to remove all probably involved tissue within the limits of reasonable surgical access; second, the steps of the operation should be so carried out that outgoing lymph streams are blocked off early in the operation, thus guarding against dissemination of malignant cells. To accomplish this last requirement Rodman emphasized the primary axillary dissection, with removal of the axillary tissue in one mass as a gland-bearing fascia.

It is possible also in the primary axillary attack to investigate the extent of metastases and to decide whether or not the complete operation is justifiable.

The standard radical operation, as carried out at the Guthrie Clinic, involves the following points: A wide area of skin must be removed; in no case should it be less than 2 inches (5 cm.) equidistant from the growth. Rodman's primary incision is a straight incision beginning 1 inch (2.5 cm.) below the clavicle and about 1½ inches (3.7 cm.) medial to the sulcus between the deltoid and the

pectoralis muscle. It parallels the sulcus. This type of incision does not extend to the arm and obviates the possibility of scar formation which may contract and limit abduction. The axilla is exposed by dividing the tendons of the pectorales at their insertions. As a rule the clavicular portion of the pectoralis major is not removed unless the growth is in the upper cut portion of the breast. The acromiothoracic and the long thoracic arteries run parallel (above and below, respectively) to the tendon of the pectoralis minor muscle and should not be injured during this step of the operation. By the cutting of the costocoracoid membrane the space of Mohrenheim is well exposed.

The dissection of the axilla begins at the apex and extends from above downward and from within outward. As the sheath and the fat are removed from the axillary vessels, the acromial long branch, the alar thoracic branch and the subscapular branch of the axillary artery are encountered in the order named. These, with their accompanying veins, are drawn out and the proximal ends ligated. No attempt should be made to remove individual enlarged glands. The contents of the axilla should be removed en masse as a gland-bearing fascia. When this dissection has been completed nothing is left on the inner aspect of the axilla but the posterior thoracic nerve of Bell and, posteriorly, the long subscapular nerve.

The breast is removed by an incision beginning at the middle of the primary incision, encircling the breast and extending downward to a point halfway between the ensiform appendage and the umbilicus. The oval should be 5 or 6 inches (12 to 15 cm.) or more at its greatest breadth, and the incision should never come within 2 inches (5 cm.) of the edge of the growth. The subcutaneous tissues are cut on a slant so that the skin in every direction is undermined for a distance of several inches from the edges of the wound.

American as well as English surgeons, following the precept of Handley, are practicing extensive deep resection of the fascia in order to prevent peritoneal invasion by malignant cells, which extends along fascial planes, particularly the rectus. The prevention of dissemination and contamination during the operative procedure is also a matter of prime importance. Dissemination may take place during the operation through uncut lymphatics, and for this reason manipulation or squeezing of the breast should be carefully avoided. Important in this consideration is the suggestion of Willy Meyer, who began the operation in the axilla, dividing the lymph vessels at their highest point before the breast was handled at all. Thus the routes of dissemination were cut off.

Jackson²² believed contamination to be the cause of local recurrence in many cases. Malignant cells escape from the lymph channels of the breast and, becoming implanted in the wound after closure, readily develop into new growths. While this idea is not demonstrable, it is plausible. To prevent such contamination, the flaps, as they are dissected laterally, are reflected and covered with wet packs, and as the dissection proceeds more packs are added, going down on the chest wall. This serves a double purpose, as much heat is prevented from radiating from the large denuded surface and the degree of shock is thereby lessened.

Closure of the wound is begun where the first incision was made, near the clavicle; closure of the oval is begun at the sternal end. After advancing one-third of the distance it can be determined whether the flaps can be approximated readily. If this is impossible the axillary portion of the wound is closed for one-

22. Jackson, J. N.: The Requirements of Technique in Operations for Cancer of the Breast, *Ann. Surg.* 72:181, 1920.

third of the distance. The central one-third, which can not be approximated, is covered by Thiersch grafts taken from the thigh. Drainage is not employed except when the patient is fleshy or when the field is wet. Early active motion is encouraged.

In conclusion, a significant group of figures is presented. One may assert that the greatest advance in the past decade both in securing improved results and in saving life lies in the fact that patients come earlier to the surgeon for treatment. That patients do come earlier is obvious when one studies the comparative statement of the average duration of the disease from the time of appearance of the first symptom to the time of the operation (table 3).

This result may in part, at least, be attributed to the work of the American Society for the Control of Cancer. It is earnestly hoped that further advances will be made in the knowledge of the nature of cancer, in methods of diagnosis and in improved treatment by operation, but it is certain that by far the most effective means of saving life and

TABLE 3.—*Duration of Mammary Cancer Before Operation*

	1910-1922	1923-1935
Average duration	65 weeks	55 weeks
Patients who came to operation within 1 year.....	43.3%	55.5%
Patients who came to operation within 6 months.....	31.4%	40.4%
Patients who came to operation within 1 month.....	7.2%	23.2%

ameliorating suffering from cancer of the breast at the present time lies in the early diagnosis of the lesion and its prompt removal by radical means.

SUMMARY AND CONCLUSIONS

Perhaps no disease has received more intensive study than has cancer. Yet it is generally agreed that cancer, one of the chief destroyers of mankind, remains essentially a mystery.

Chronic mastitis, stagnation, previous involutional or inflammatory changes and trauma are believed by many to be important predisposing conditions.

Malignant tumor of the breast is especially prevalent in the fourth and fifth decades of life. It is seldom found in persons under the age of 20 years.

About 1 per cent of malignant tumors of the breast are found in male patients.

Cystic disease is not believed to be a precancerous lesion, and malignant changes are no more likely to develop in a breast showing the disease than in one which is entirely normal.

All single solid tumors of the breast should be removed for diagnosis. While the diagnosis of carcinoma can in the majority of cases be made from the gross tissue at the operating table, a competent pathologist with facilities for examining frozen sections should be available for the 10 or 20 per cent of cases in which this is not possible.

Mammary cancer is found more often in married women than in unmarried women. This comparative frequency prevails to such an extent that one suspects that the incidence of mammary cancer in married women is dependent on some definite factor.

Cancer of the breast seems to appear slightly earlier in those patients who are unable to meet the physiologic demands of pregnancy and latest in those who have never been pregnant.

Cancer can be cured, but early diagnosis and appropriate treatment are absolutely necessary. Thousands of persons with lesions of proved malignancy have been restored to health for periods up to ten or more years through surgical treatment or irradiation, alone or in combination. Biopsy of material taken from questionable lesions is by far the best policy.

Salient features to be considered in differentiating between benign lesions and cancer are presented from the clinical and gross pathologic standpoint.

Cases in which there is involvement of the lymph glands decidedly outnumber those in which there is no such involvement. In the former group the mortality at the end of ten years is about four times that in the latter group.

Definite metastases in the supra-clavicular region are a contraindication to surgical treatment, as is also large extension to the axilla, because, first, life is endangered and, second, discredit may be brought to surgery in the minds of the laity.

Continued education of the laity is one of the best weapons in the fight against malignant tumors. One often hears the remark made that publicity and propaganda do more harm than good, because of the alarm and terror they may arouse in an ignorant and unintelligent public. The argument is specious. The imaginary horror is not nearly so harmful as the actual terror that accompanies malignant disease.

At present, radical operation for cancer of the breast permits a number of different incisions but is commonly understood to demand the removal in one piece of the following structures: the breast (with all the skin over the breast), the pectoralis major and pectoralis minor muscles, the axillary contents (with the exception of the vein, the artery and the brachial plexus) and the deep fascia from clavicle to epigastrium and from sternum to latissimus.

Patients during the last decade have been coming to operation earlier by a few weeks than those of the previous ten years.

PROBLEMS IN THE SURGICAL TREATMENT OF RENAL CALCULI

THOMAS E. GIBSON, M.D.

SAN FRANCISCO

Montaigne, the great philosopher of the sixteenth century, has given a most graphic description of the symptoms of "stone," tinged by the unmitigated reality of personal experience, since he himself was a sufferer for many years:

Thou art seen to sweat with pain, to look pale and red, to tremble, to vomit well nigh to blood, to suffer strange contortions and convulsions, by starts to let tears drop from thine eyes, to urine thick, black, and frightful water, or to have it suppressed by some sharp and craggy stone that cruelly pricks and tears thee.

However, he never reached "such a degree of despair as to bellow and make uproar." He traveled much, seeking a cure at the various watering places of Europe, but without success.

Through the centuries the cause of the formation of stone remained obscure. However, during the last few years knowledge of the causes and prevention of urinary lithiasis has been greatly augmented by painstaking research on the part of numerous investigators. This knowledge has served to emphasize the fact that the surgical removal of stone from the urinary tract is but incidental to a general plan of treatment. The occurrence of stone must be considered a manifestation of some underlying disease, and every effort should be made to discover what etiologic factors are responsible in the individual case. After the elimination of calculi from the urinary tract intelligent follow-up treatment must be carried out to prevent recurrence.

The present highly developed instrumental armamentarium and diagnostic equipment have made exploratory operations on the genito-urinary tract practically obsolete. With accurate diagnosis at his command, the surgeon's mind should be made up before he operates, and not at the operating table. However, with respect to urinary calculi, the choice of treatment often presents problems which tax the ingenuity, experience and skill of the urologist to the utmost. The surgical treatment of renal calculi often presents difficulties, certain phases of which perhaps have not been sufficiently stressed. For this reason, a few of the surgical problems arising in the course of my personal experience are presented for consideration.

THE MEDIUM-SIZED CALCULUS IN THE RENAL PELVIS

Probably the easiest of all operations on the kidney is the removal of the uncomplicated medium-sized stone (from 1 to 3 cm. in dimensions) from the renal pelvis (fig. 1). Provided the ureter and pelvis are not surrounded by dense adhesions (periureteritis and peripyelitis) and no obstructive factor is present necessitating plastic repair of the pelvic outlet, simple pyelotomy is all that is necessary. In the absence of gross infection the incision is closed tightly with interrupted sutures of fine catgut and drainage is limited to a Penrose tube down to the region



Fig. 1.—Stone in the pelvis of the right kidney: (A) plain roentgenogram of kidney, ureter and bladder; (B) pyelogram. This is a case without complications, suitable for simple pyelolithotomy.

of the pelvis in order to take care of urinary leakage, which may last a few days or may not occur at all.

SURGICAL PROBLEM OF THE SMALL RENAL CALCULUS

No operation on the kidney is approached with as much trepidation in my personal experience as the removal of the small, freely movable stone in the renal pelvis (fig. 2). The smaller the stone or stones the greater is the anxiety. Having seen surgeons on one or two occasions acknowledge failure after a search for a small stone in the kidney, I have gained a wholesome respect for such offenders. They are often

capable of causing greater pain than the larger stones; hence all the more reason for finding and removing them. The problem of locating them may well be likened to the proverbial searching for a needle in a haystack, at least in some cases.

No operation for renal or ureteral stone should be undertaken without a plain roentgenogram taken immediately before the operation. The film should be hung in the operating room to guide one's approach to



Fig. 2.—Small ball valve stone in the pelvis of the left kidney. The small renal stone often presents a difficult surgical problem because it may be elusive.

the stone. However, manipulation of the kidney incidental to exposure may cause the stone to shift its position and retreat into the dark recesses of the kidney, where it may elude probing or palpation through a pyelotomy incision. In exposing the kidney, one should as soon as possible isolate and occlude the ureter below the pelvic outlet to prevent possible escape of the stone in that direction. In case the stone cannot be found on careful exploration through the incision in the renal pelvis a roentgenogram of the kidney at the operating table may be of material

assistance in locating it. However, even this assistance may be of no avail, as happened in the case illustrated in figure 2.

The patient was a young woman with severe colic resembling epileptiform convulsions, poorly controlled by morphine and atropine in generous doses. A ureteral catheter relieved pain by pushing the stone away from the pelvic outlet, but recurrence of pain soon followed the removal of the catheter. The description of the operation (Nov. 26, 1928) is as follows: A subcostal incision was made running from the costovertebral angle anteriorly and downward for a distance of about 5 inches (12.5 cm.). Incision was continued through the muscles to the retroperitoneal fascia, no nerves and practically no bleeders being encountered. The costovertebral ligament was cut in order to give adequate exposure. When the retroperitoneal fascia was opened, the lemon yellow fat about the kidney was seen. The lower pole of the kidney and in turn the ureter were readily exposed. A $\frac{1}{2}$ inch (1.3 cm.) tape was passed beneath the ureter to serve for traction. The ureter was followed up toward the kidney, and a small pelvis, intrarenal in type, was found. There was some reaction about the pelvis, so that it was difficult to get a good exposure until the adhesions had been broken up and the bleeding stopped. Two 00 catgut retention sutures were placed in the pelvis just above the ureteropelvic junction and a small incision made between them. In an attempt to grasp the stone with forceps through the incision it was pushed up into the renal pelvis, and it was impossible to locate it again. It was a small stone, less than 0.5 cm. in diameter. Ordinarily such a stone would pass down the ureter, but because the patient had been suffering terrible agony for two weeks and the stone had not got further than the ureteropelvic junction, it was deemed advisable to remove it surgically.

The upper pole of the kidney was then freed and the kidney brought into the wound. Still careful palpation and probing failed to locate the stone. Therefore, the roentgenologist was called in, with his portable machine, and an exposure was made to try to determine the new location of the stone. In the picture thus made the stone showed clearly and from all appearances seemed to be still in the pelvis. Probing through this opening failed to reveal it. A Mayo hemostat was introduced through the opening, and no grating sensation of the stone could be felt anywhere. When the hemostat was withdrawn a clot of blood was seen to protrude from this opening. This was removed and another attempt made to palpate the stone in the kidney. While this was being done the nurse discovered the stone buried in the middle of the clot which had just been removed. The clot of blood completely disguised the stone and made it impossible to detect it by palpation or to get any grating sound on a metal instrument. After this fortunate occurrence closure was begun. The two incisions in the pelvis and ureter were closed with 00 catgut sutures, a piece of fat being placed over the incision and tied in with a suture. A tubular rubber dam for drainage was placed in the region of the renal pelvis and brought out through the posterior angle of the wound. The muscles were closed in two layers with continuous lock sutures of no. 2 chromic material. The subcutaneous tissues were approximated with interrupted sutures of 00 catgut. Skin was closed with a continuous lock suture of dermol. The wound was dressed with tincture of benzoin. The patient was given a hypodermoclysis on the table and returned to her room in good condition.

Here was an urgent and clearcut indication for operation, and yet the stone could not be found. When I was about to give up in despair the nurse at the operating table said, "Here it is" and showed me the

stone extracted from a small blood clot which had been removed from the renal pelvis. The nurse was properly rewarded for her alertness, and my respect for the small renal calculus was further enhanced.

A similar problem arose in connection with the case illustrated in figure 3.

To make matters worse, the renal pelvis was intrarenal in type, so that the little finger could not be inserted in the hope of palpating the stone. Furthermore, the stone eluded the grasp of the forceps, and no grating sensation could be elicited by probing into the calices. As a last resort the hydraulic maneuver illustrated in figure 4 was utilized, with gratifying results. A small soft rubber catheter was inserted into the renal pelvis, and the pyelotomy incision was closed tightly about

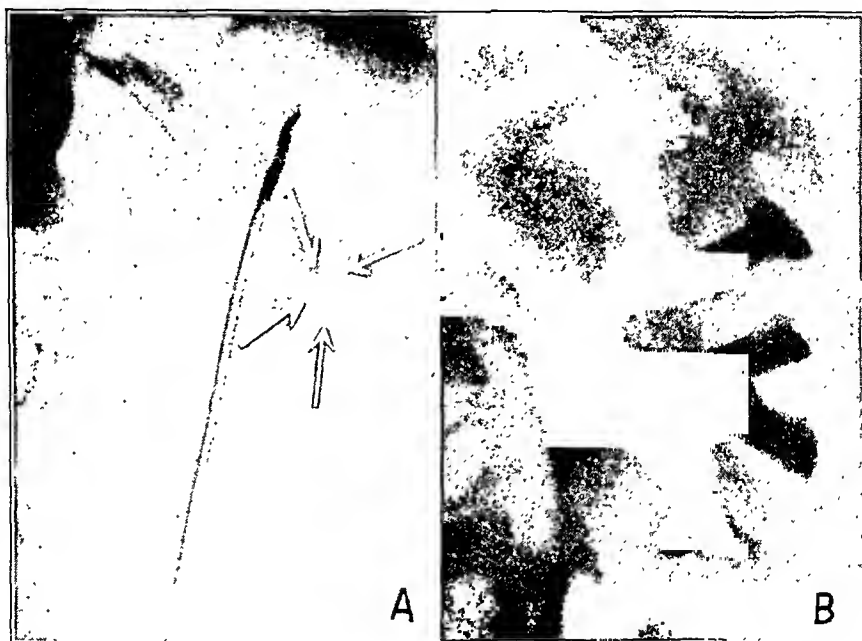


Fig. 3.—Small renal stone (*A*) in pelvis of kidney (*B*). The pelvis is intrarenal in type and the stone freely movable, having ready access to all the calices. The surgical problem of finding such a stone may be most difficult unless one resorts to the hydraulic maneuver described in the text and illustrated in figure 4.

the catheter by pressure of thumb and forefinger, while an assistant with a 10 cc. Luer syringe injected physiologic solution of sodium chloride with some force. When the pelvis and calices were fully distended the catheter was suddenly withdrawn. The sudden outrush of fluid created a strong outward current, which carried the stone with it. The stone was found (to the great relief of all present) reposing on the gauze sponge previously placed beneath the renal pelvis.

The point which makes the difference between success and failure in the hydraulic maneuver is that the same principles must be followed as in the evacuation of small stones or fragments of stones from the bladder following litholapaxy. It does not suffice to insert a catheter or

the point of a syringe into the pelvis and flush the kidney. The solution merely runs back out of the pyelotomy incision around the catheter or syringe. The incision must be kept closed tightly while the injection is made, and it is preferable to flush back and forth just as with the bladder evacuator, in order to set up a current of sufficient force within the kidney to set the stone in motion. Then during the phase of complete distention the syringe or catheter is suddenly removed and the outrushing of fluid allowed to carry the stone with it. Figure 5 illustrates

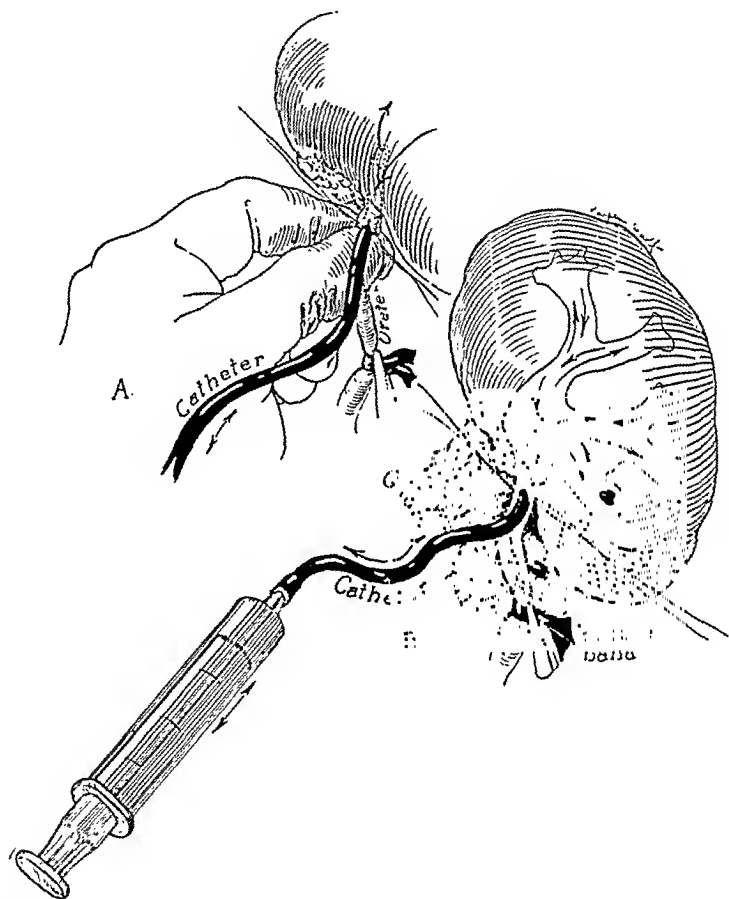


Fig. 4.—Technic of the hydraulic maneuver, of value in removing the small renal calculus which escapes detection by other means. This procedure was used in the case illustrated in figure 3. The pelvis is intrarenal in type, a circumstance which always makes the surgical problem more acute. The same principles apply here as in the evacuation of small stones or fragments of stone from the bladder. Note that in *A* the thumb and forefinger keep the opening in the ureter tightly closed to prevent the escape of the fluid around the catheter while the injection is being made. Forceful to and fro movements of the piston (shown in *B*) set the stone in motion. After a final forcible injection the catheter is suddenly withdrawn, and the stone is carried out through the opening in the ureter with the outrushing current of fluid and is seen reposing on the gauze sponge beneath the ureter.

the use of an asepto syringe in the extrarenal type of pelvis. Probably an ordinary ear syringe would be even more satisfactory, but I have not had occasion to use it. Figure 6 represents a purely theoretic application of the McCarthy evacuator in cases of hydronephrosis with multiple small calculi. The hydraulic maneuver, if it may be dignified

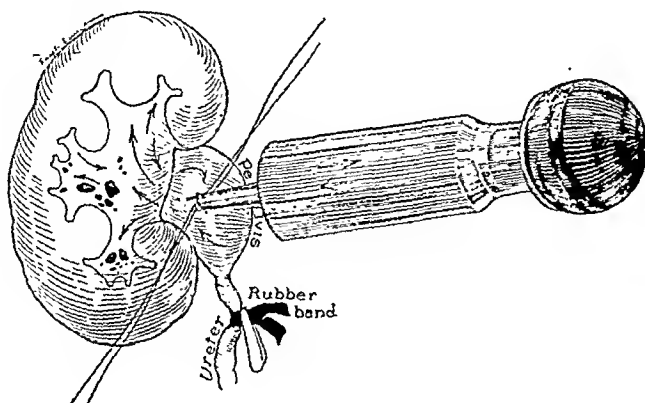


Fig. 5.—Application of the principle illustrated in figure 4 to a case of multiple small calculi in which the pelvis is of extrarenal type. An ordinary asepto bulb syringe was used.

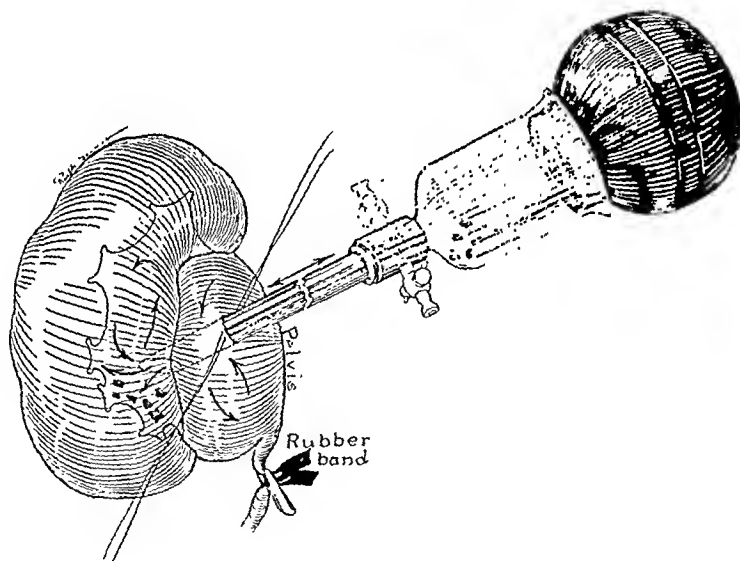


Fig. 6.—Hypothetic use of the McCarthy evacuator in a case of small calculi in a large hydronephrotic kidney.

by such a term, not only is of great value in dealing with the small, elusive renal calculus but should occasionally prove valuable in the eviction of unsuspected stones. Braasch and Foulds (1923) in reviewing 1,079 operations for stone noted that multiple stones were found at operation in 146 cases in which a single shadow was seen in the roentgenogram.

URETHRAL SPLINT AS APPLIED TO PROBLEM OF FORMATION
OF STRICTURES WITH SECONDARY HYDRONEPHROSIS
AFTER PYELOLITHOTOMY

Not infrequently one is surprised to find a presumably easy pyelotomy for stone complicated by dense adhesions about the upper part of the ureter and the renal pelvis. Routine urologic investigation prior to operation may give no inkling of their presence, which may make an otherwise simple operation very difficult. It is in cases of this sort particularly that unfavorable late results occur in the form of refractory or impenetrable stricture and ultimate destruction of the kidney by secondary hydronephrosis. The patient may have no symptoms, and such a result may pass unrecognized unless urographic studies are made after operation. Patients are prone to think that an operation should end the necessity for instrumental manipulation, and deference to their objections often influences the urologist to neglect this extremely vital follow-up program, with the result that in an occasional case the kidney becomes permanently damaged or functionless. A few unfortunate experiences of this sort have convinced me that no patient should be allowed to leave the hospital after pyelotomy or ureterotomy without ureteral catheterization and dilation and pelvic lavage to be sure the ureter is free from kinks and strictures and that no residual infection remains to favor the recurrence of stones and the development of hydronephrosis. As a further precautionary measure to prevent such disastrous end results, I believe the use of the ureteral splint at operation is definitely indicated, at least in all cases in which evidence of previous periureteritis and peripyelitis exists in the form of dense adhesions about the ureter and pelvis. An indwelling ureteral catheter may be placed cystoscopically before operation, and if deemed advisable a second catheter may be passed in a retrograde manner during the operation and left in place for several days postoperatively so as to secure a straight ureter with good drainage and to prevent kinking, formation of stricture and urinary stasis.

The result of neglecting these fundamental principles is well shown in the 2 cases illustrated in figures 7 and 8.

Pyelolithotomy in both cases was rendered difficult by the presence of dense adhesions about the upper part of the ureter and pelvis. No ureteral splinting was utilized at operation. As a result marked distortion and stenosis of the upper part of the ureter and of the pelvis developed in both cases, with resultant hydronephrosis. In 1 (fig. 7) after several attempts the renal pelvis was successfully entered by ureteral catheter through the cystoscope. In the other (fig. 8) all attempts proved unsuccessful, and nephrectomy for infected hydronephrosis was later necessary.



Fig. 7.—Small renal calculus offering a difficult surgical problem for pyelolithotomy because of the small intrarenal pelvis surrounded by dense adhesions due to chronic periureteritis and peripyelitis. The ureteral splint is recommended routinely in such cases. Failure to use the ureteral splint in this case resulted in stricture and distortion of the pelvis and ureter with secondary hydronephrosis following the operation. Dilators were passed after numerous cystoscopies, and the kidney was saved from complete destruction only with the greatest difficulty.

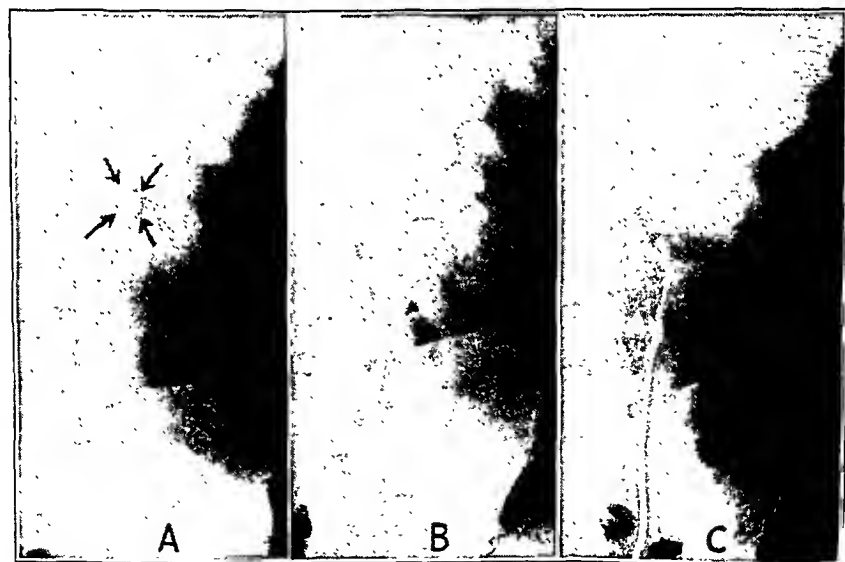


Fig. 8.—Calculus in the pelvis of the left kidney: *A*, plain roentgenogram; *B*, pyelogram. Dense adhesions about the pelvis made the removal of the stone difficult, and failure to make use of the ureteral splint resulted in imperforate stricture of the ureter (*C*) and infected hydronephrosis later requiring nephrectomy.

The ureteral splint may be used in several ways. The catheter may be passed before operation to the renal pelvis through a cystoscope, or a retrograde catheter may be passed down the ureter from above through the pyelotomy wound. Drainage by means of nephrostomy may be combined with ureteral splinting as shown in figure 9 *a* and is advisable in cases of severe infection as well as in all anastomotic procedures and certain types of plastic repair of the ureter and pelvis. Figure 9 *b* shows a method of ureteral splinting without nephrostomy.

This procedure was used in a case of hydronephrosis without infection due to stricture of the pelvic outlet, in which stones were of secondary importance. The lower part of the hydronephrotic sac was cut away, the stones included, the pelvic outlet dilated with a Mayo hemostat and multiple vertical incisions made about it down to the submucosa, as described by David M. Davis (1933), the principle of

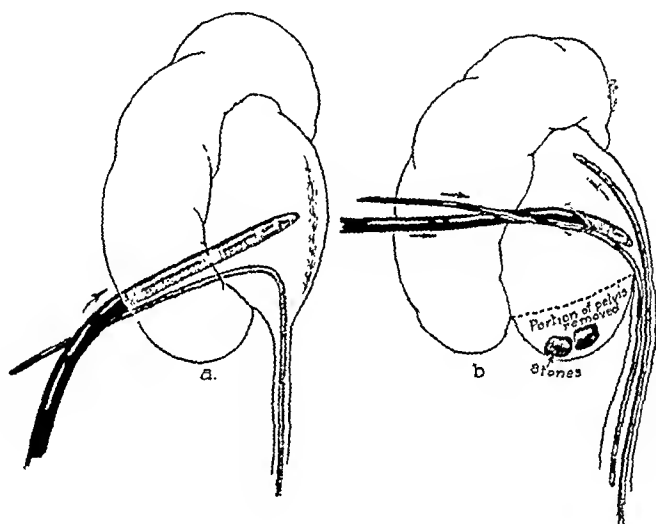


Fig. 9.—Types of ureteral splinting: (*a*) with drainage by means of nephrostomy, (*b*) with drainage by means of pyelotomy. Splinting is advisable in practically all cases of plastic repair of the pelvis or ureter and in all operations for stone in the kidney or ureter associated with periureteritis or peripelitis. The ureteral catheter is generally the best splint and should be retained in place for a week or more, according to the need of the patient. Use of the principle of the splint will insure a straight ureter and adequate renal drainage. The procedure shown in *b* was followed with excellent results in the case illustrated in figure 10.

the Rammstedt operation for pylorospasm being utilized. Two no. 7 F ureteral catheters were inserted as a ureteral splint and to maintain dilatation of the pelvic outlet. They were left in place six days. The pyelograms (fig. 10) show the condition before operation and the final result seven months after operation.

The ureteral splint is of great value also in preventing distortion and stenosis following operations for stone in the lower ureter (fig. 11), particularly where there is much periureteral reaction. It is advisable

to pass a catheter at cystoscopy before operation, to be left in place during and after operation. If the catheter cannot be passed beyond the stone through the cystoscope, one can pass it on up to the renal kidney pelvis at operation after the stone is removed.

In a case such as that illustrated in figure 11, in which the stone is close to the bladder and a catheter cannot be passed from below, one can follow the procedure used in that case:

After the stone was removed at operation, one end of a ureteral catheter was passed upward to the renal pelvis and the other downward into the bladder through the ureterotomy wound. After six days the end of the catheter which was coiled in the bladder was brought out through the urethra with the aid of the cystoscope.

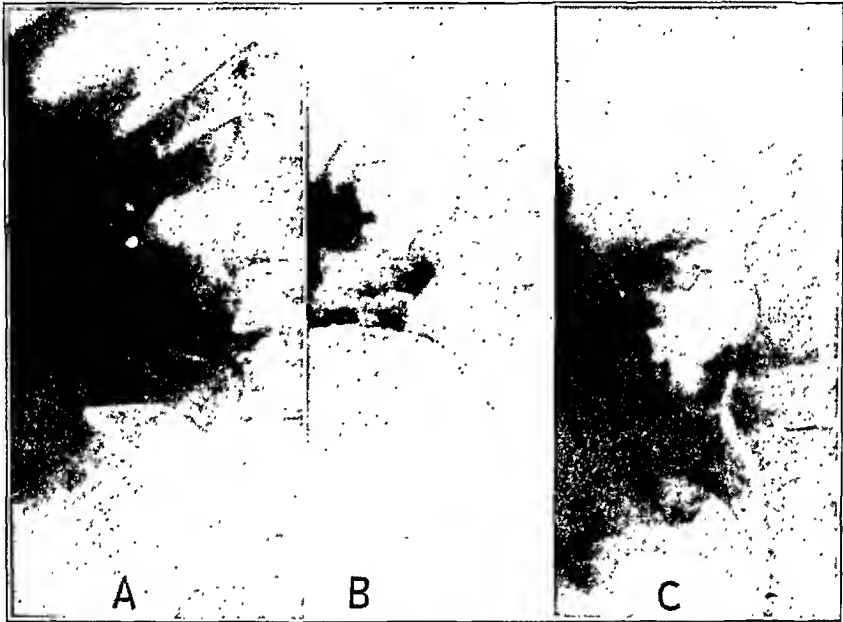


Fig. 10.—Two small calculi (*A*) in the pelvis of a right hydronephrotic kidney (*B*). Hydronephrosis was due to stricture at the pelvic outlet. The operation carried out in this case is shown in figure 9 *b*. In addition, the pelvic outlet was thoroughly dilated with a Mayo hemostat and vertical incisions made externally about the ureteropelvic junction down to the submucosa to allow of maximum patency. A double ureteral catheter was used as a splint and left in place for a week after operation. This kidney also exhibited marked ptosis in the vertical pyelogram, which was corrected by nephropexy. Since the patient was an extremely neurotic young woman, a renal sympathectomy was done to make doubly sure of relieving all pain. The ultimate result is shown in *C* seven months after operation. The kidney has regained perfect function and is free from infection.

Use of the ureteral splint in such cases will definitely prevent the occurrence of distortion, stenosis and urinary fistula, which sometimes make it difficult or impossible to pass a catheter up the ureter afterward.

PROBLEM OF CHOICE OF NEPHROTOMY, HEMINEPHRECTOMY OR
NEPHRECTOMY IN CASES OF LARGE STONE

The remarkable reparative power of the kidney has impressed urologists of late years, and a conservative trend has grown in renal surgery. Kidneys practically devoid of function are seen to recover to a surprising degree when conscientious treatment is undertaken before operation to eliminate infection and promote free drainage in cases of renal stone complicated by infection and obstruction. Even in cases in which these factors are not present to any degree, the presence of a stone in the kidney appears at times to exert an inhibitory action on



Fig. 11.—Bilateral hydronephrosis, on the right due to ureteral stricture and on the left to two calculi, which appear as one in the lower part of the ureter near the bladder. The stones were removed by a midline ureterolithotomy. A ureteral catheter could not be passed beyond the stones with the cystoscope but was inserted, for the purpose of splinting, through the incision after the stones were removed, one end being passed into the bladder and the other up to the renal pelvis.

function, and at operation one will be surprised to find an amount of healthy-looking parenchyma far beyond expectations based on previous studies of function. Realization of these factors will sometimes result in the saving of a kidney in a case in which nephrectomy was contemplated. Figure 12 illustrates the ideal type of case for partial resection of the kidney rather than nephrectomy in the treatment of renal calculus.

There was a large stone in the pelvis and in addition one in the lower major calix with evidence of gross infection and dilatation about it. The upper half of the kidney was remarkably normal. The best interests of the patient were served by removing this diseased renal tissue with the stones.

Figure 13 illustrates a case in which a large stone was present and in addition the entire kidney was heavily infected, with complete loss of function.

A nephrolithotomy was done with drainage by means of nephrostomy, but the infection did not clear up, and there was no return of function. In this case the treatment employed was too conservative, as later events proved a nephrectomy would have been the procedure of choice.



Fig. 12.—Large stones in an ideal case for resection of kidney; *A*, plain roentgenogram of kidney, ureter and bladder; *B*, pyelogram showing their relation to the kidney. The lower pole of the kidney presented a localized pyonephrosis. The abscess about the stone in the lower pole is readily seen in the pyelogram. The parenchyma of the lower pole was destroyed by chronic inflammatory changes. Since the upper two thirds of the kidney appeared normal, the lower third was resected and all the stones removed through this approach. The patient made an excellent recovery.

One must judge from the appearance of the parenchyma at operation and not be influenced entirely by the preliminary urinary and functional findings as to whether to do a nephrectomy or a nephrotomy. Figure 14 illustrates a case in which renal function before operation as measured by the output of phenolphthalein was almost nil, yet after operation there was a return to normal.



Fig. 13.—Large left renal calculus: *A*, plain roentgenogram of kidney, ureter and bladder; *B*, pyelogram. The stone was removed by nephrotomy, but severe damage to the parenchyma from chronic infection and failure of any functional restoration later proved that nephrectomy would have been the procedure of choice in this instance.

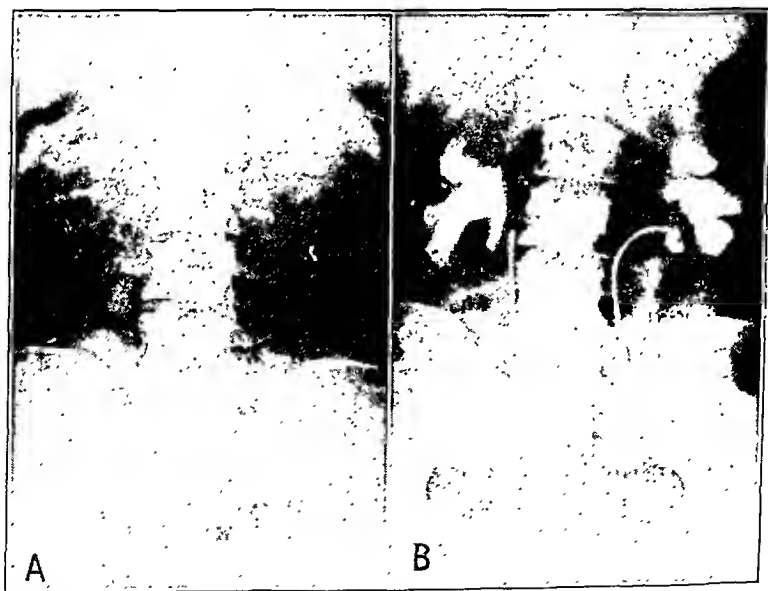


Fig. 14.—Stone in the left kidney in the case of young woman: *A*, plain roentgenogram of kidney, ureter and bladder. The condition was associated with bilateral ptosis, marked kinking of ureters and advanced hydronephrosis on the left, with greatly impaired function. Pyelolithotomy and nephropexy were successfully performed, and the function returned to normal.

PROBLEMS ASSOCIATED WITH BILATERAL RENAL CALCULI

In figures 15 and 16 are shown successive stages of the formation of stones in a woman of 24.

First of all a stone lodged in the left ureter. Attempts to encourage it to pass resulted in perforation of the left ureter with perirenal extravasation of infected urine. A culture of the blood was positive for *Bacillus coli*. Drainage was instituted through a lumbar incision, and healing occurred after the stone had passed. After this episode a large stone blocked the right ureter. Several smaller stones were present in the right kidney. The right ureteral orifice was slit with ureteral scissors. This procedure was followed by a hemorrhage which filled the bladder with clots and necessitated instrumental evacuation. The stone in the right ureter passed, followed by the smaller ones above. There was marked infection in both kidneys, and every effort was made by diet, medication and frequent renal lavage to clear it up, but without success. During the next year a large stone formed in the left kidney. This was removed by nephrotomy, which was followed by use of a ureteral splint and drainage by means of nephrostomy. During operation hemorrhage from the nephrostomy wound was controlled by a tourniquet on the renal pedicle, consisting of a soft rubber no. 20 urethral catheter held by an assistant. I believe this method is far safer, and endangers the integrity of the kidney less, than the use of any kind of clamp. The operation was difficult owing to the presence of adhesions from the perirenal extravasation of a year before. The wound made by nephrotomy was closed by the ribbon gut method of Lowsley, which appears to be a distinct improvement over the old method of mattress sutures through the substance of the kidney. The infection in both kidneys cleared up promptly, and the function on both sides is now practically normal.

An extreme example of bilateral calculus disease is illustrated in figure 17.

The patient was a woman of 40 with large calculous pyonephrosis associated with perinephric abscess on the left side. On the right side was a calculous pyonephrosis in the lower half of the right double kidney. The excretion of phenolsulfonphthalein was 40 per cent for two hours. The patient was emaciated and practically moribund. A nephrectomy on the left side was done in two stages. The first stage consisted of nephrostomy and drainage of the perinephric abscess. Two weeks later nephrectomy was done. The patient improved remarkably, and in the following year her weight advanced from 84 to 170 pounds (38.1 to 77.1 Kg.). She now enjoys good health, but still retains her calculous pyonephrosis in the lower half of her double right kidney. The question now stands, Should a heminephrectomy be done on this remaining kidney or should discretion be allowed to dictate a hands-off policy? I have favored the latter alternative.

In figure 18 the findings in a woman of 36 are shown.

On the right side was a congenital infantile kidney, not much larger than a golf ball, while the left kidney contained a large staghorn calculus and had undergone replacement fibrolipomatosis. Death occurred as a result of uremia plus sudden exacerbation of infection in this kidney with the formation of perinephritic abscess, generalized peritonitis and septicemia.

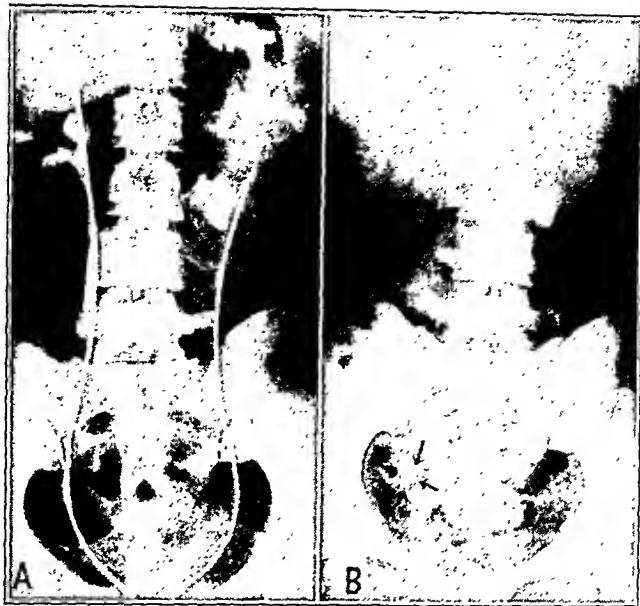


Fig. 15.—Infection with *Bacillus coli* in both kidneys and formation of multiple stones. In *A* is shown a stone in the lower part of the left ureter and the extravasation of the pyelographic medium about the pelvis of the left kidney. Urinary extravasation and perinephric abscess occurred, necessitating lumbar drainage. The stone was removed cystoscopically. One month later a large stone was seen in the lower part of the right ureter (*B*) and multiple small calculi in the right kidney. This stone was removed cystoscopically and the small ones in the kidney passed spontaneously (fig. 16). A large calcified lymph gland is seen on the left near the spine.



Fig. 16.—Large branching calculus in the left kidney in the case shown in figure 15, one year later. The large calcified gland is shown above the calculus, in a higher position than in figure 15. The calculus was removed by nephrotomy with Lowsley ribbon gut closure. The result was excellent.

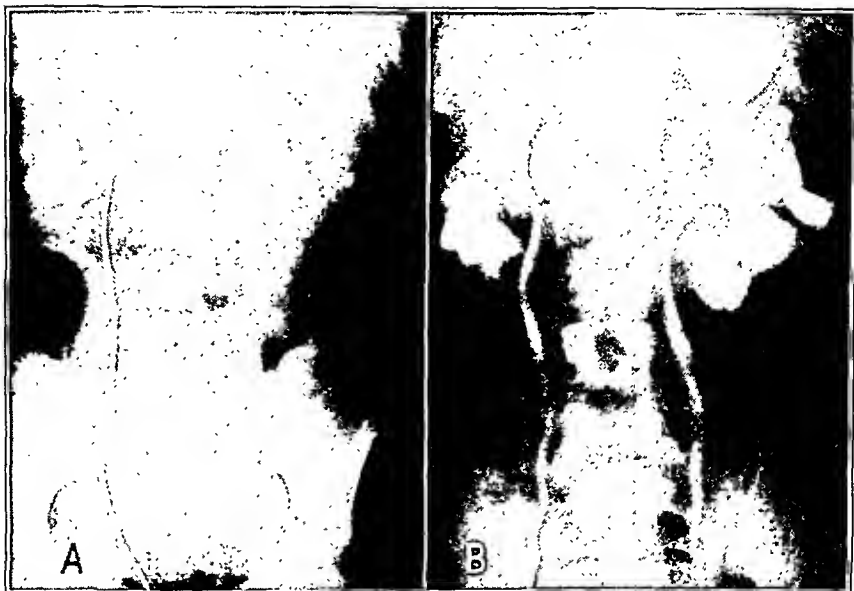


Fig. 17.—Extensive bilateral calculous disease: *A*, plain roentgenogram of kidney, ureter and bladder; *B*, bilateral pyeloureterogram. On the right side is a double kidney with calculous pyonephrosis of the lower half; on the left, complete destruction of the kidney by calculous pyonephrosis with a communicating perinephric abscess at the upper pole beneath the diaphragm. The patient depended entirely on the upper half of the right double kidney for renal function; the excretion of phenolsulfonphthalein was 40 per cent in two hours. A two stage nephrectomy was performed on the left. The patient weighed 84 pounds (38.1 Kg.); one year after the operation she weighed 170 pounds (77.1 Kg.).

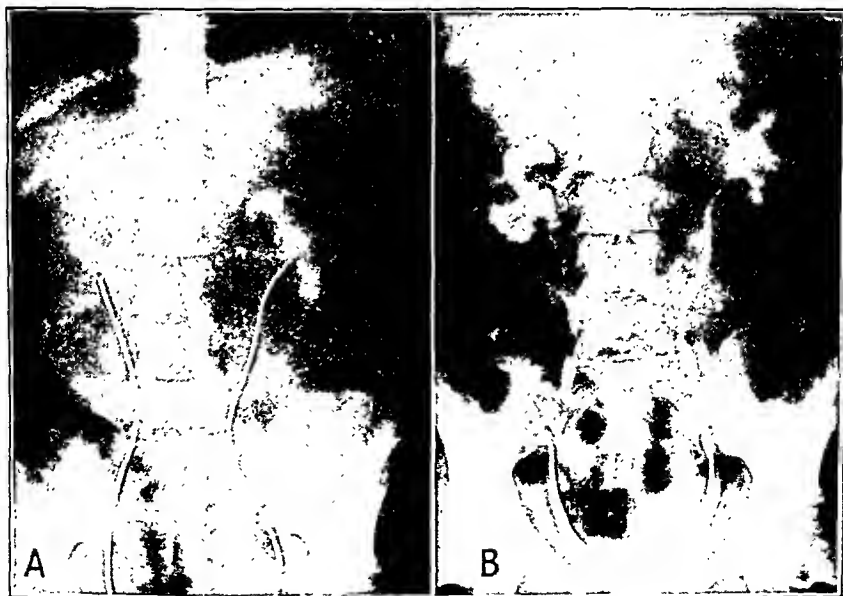


Fig. 18.—Hydronephrotic congenital infantile right kidney and left kidney devoid of function by calculous disease associated with chronic infection: *A*, plain roentgenogram of kidney, ureter and bladder; *B*, bilateral pyeloureterogram. There is also a perinephric abscess on the left side. The patient died of acute peritonitis, septicemia and uremia.

PROBLEM OF CYSTOSCOPIC MANIPULATION VERSUS OPERATION
IN MANAGEMENT OF URETERAL STONE

In figure 19 is shown a calculus in the upper part of the ureter which resisted repeated attempts to promote its passage by cystoscopic manipulation.

Finally severe ureteral colic with chills and fever developed, demanding emergency treatment. The stone was pushed back into the renal pelvis with a ureteral catheter at cystoscopy. Four years have passed since then without symptoms, but the patient still has his stone tucked away in a minor calix, and he refuses operation. Early operation would have been better than resorting to so many attempts to secure passage of the stone by cystoscopic manipulation and would have saved the patient a substantial amount of time, disability and suffering.

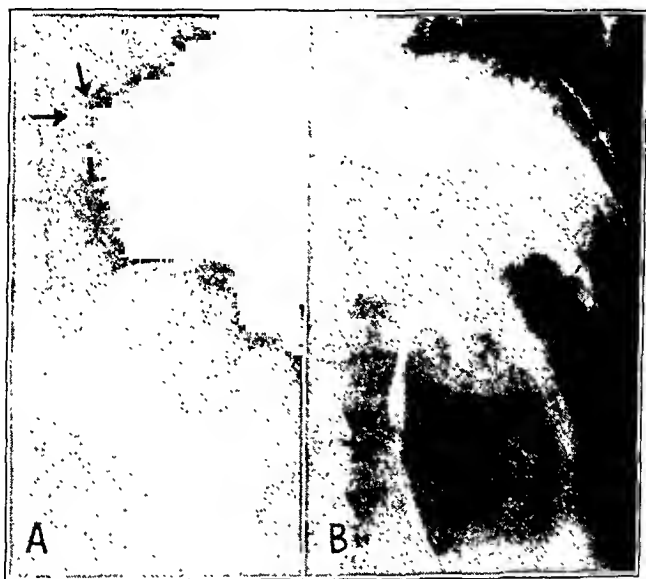


Fig. 19.—Calculus impacted in the upper part of the left ureter: *A*, plain roentgenogram of kidney, ureter and bladder; *B*, excretion urogram. Repeated cystoscopic manipulations resulted in fever and chills associated with renal colic. The stone was then pushed back into the kidney by a ureteral catheter, where it still remains after four years. Early operation would have been the procedure of choice in this case.

If a stone shows no tendency to pass after a reasonable amount of cystoscopic treatment, it should be removed surgically without further delay. Furthermore, the various types of metallic instruments, which when used judiciously in the lower third of the ureter will often remove calculi, should not be used in the upper ureter under any conditions. Figure 20 illustrates a case in which there was an attack of renal colic on the left side associated with what appeared to be a small stone in the pelvis and a moderate degree of hydronephrosis.

Nothing was done. The patient returned two and one-half years later with a second attack of renal colic. At this time a large hydronephrotic sac was found, requiring nephrectomy.

Such a case indicates the necessity for thorough urologic study and close surveillance in cases of seemingly minor pathologic conditions in order to prevent the eventual destruction of a kidney.

GAS GANGRENE FOLLOWING OPERATION FOR STONES

Fortunately gas gangrene following operation on the kidney for stone is extremely rare, but it may happen most unexpectedly. Figure 21 illustrates a case in which it occurred.

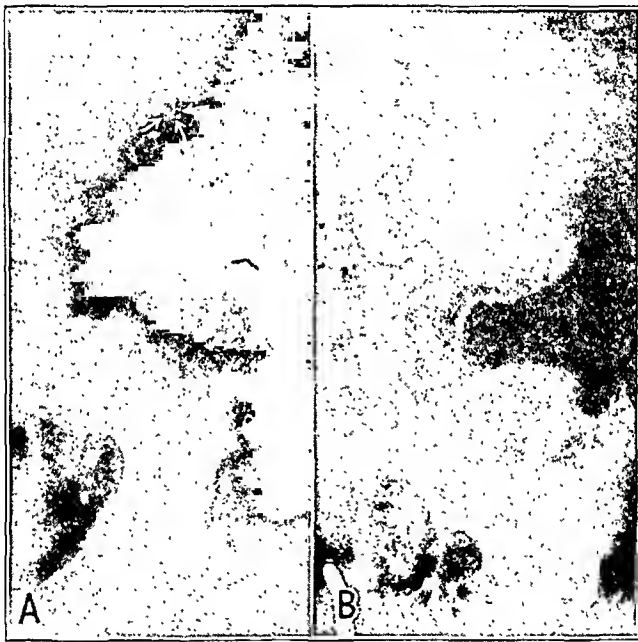


Fig. 20.—Moderate hydronephrosis (*A*) associated with what appears to be a small stone in the lower major calix. The patient refused treatment and came back two and one-half years later with renal colic and a large hydronephrotic sac (*B*) requiring nephrectomy.

Prior to operation the patient suffered with a severe attack of pyelonephritis, and on passage of a large (8 F) ureteral catheter the pus was found too thick to drain through the catheter without diluting it with physiologic solution of sodium chloride. The catheter was left in place for a week and the renal pelvis frequently washed with antiseptics. When the patient's temperature had been normal for several days and the infection was apparently pretty well cleared up, a pyelolithotomy was done and was followed by typical gas gangrene of the wound. Fortunately it responded to anti-gas gangrene serum and the patient recovered.

Recent work has shown the efficacy of roentgen therapy and sulfanilamide in the treatment of gas gangrene, which may rob it of some of its terrors.

HYPERPARATHYROIDISM WITH NEPHROLITHIASIS

In a small percentage of cases hyperparathyroidism is the chief etiologic factor in the formation of renal calculi. This factor is of such importance that the calcium and phosphorus content of the blood should be determined as a routine part of every investigation involving urinary calculi. Figures 22 and 23 illustrate successive stages of formation of stone in such a case.

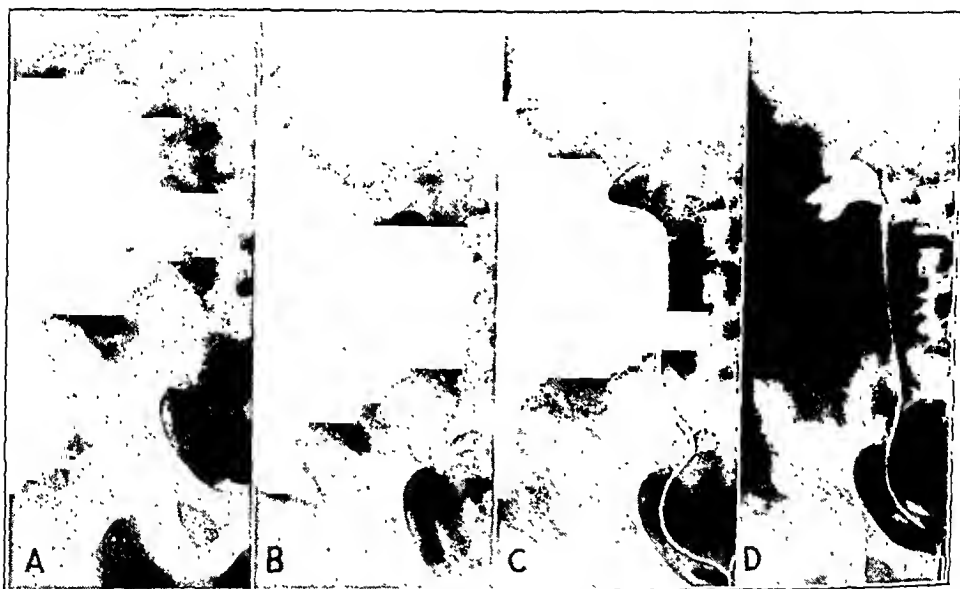


Fig. 21.—Gas gangrene following pyelolithotomy: *A*, plain roentgenogram of kidney, ureter and bladder; *B*, pyelogram. The kidney showed no function, and pus was so thick in the renal pelvis that it would not come through a catheter without dilution. An indwelling ureteral catheter was placed one week before pyelolithotomy. *C*, plain roentgenogram of kidney, ureter and bladder; *D*, pyelogram, three years later. The renal function had returned practically to normal, and no infection was present.

The patient, a man aged 44, was first operated on for a stone blocking the lower part of the left ureter. Roentgenograms showed multiple calculi in both kidneys, including the seedlike concretions in the parenchyma which are characteristic of this disease. After ureterolithotomy, the patient's neck was explored, and a large parathyroid adenoma, weighing slightly more than 10 Gm., was removed. However, the calcium and phosphorus content of his blood did not return to normal as had been hoped. Subsequently, large stones blocked the right ureter, and a second ureterolithotomy had to be done. Later a stone again blocked the left ureter, at the site of the original ureterolithotomy. Cystoscopic

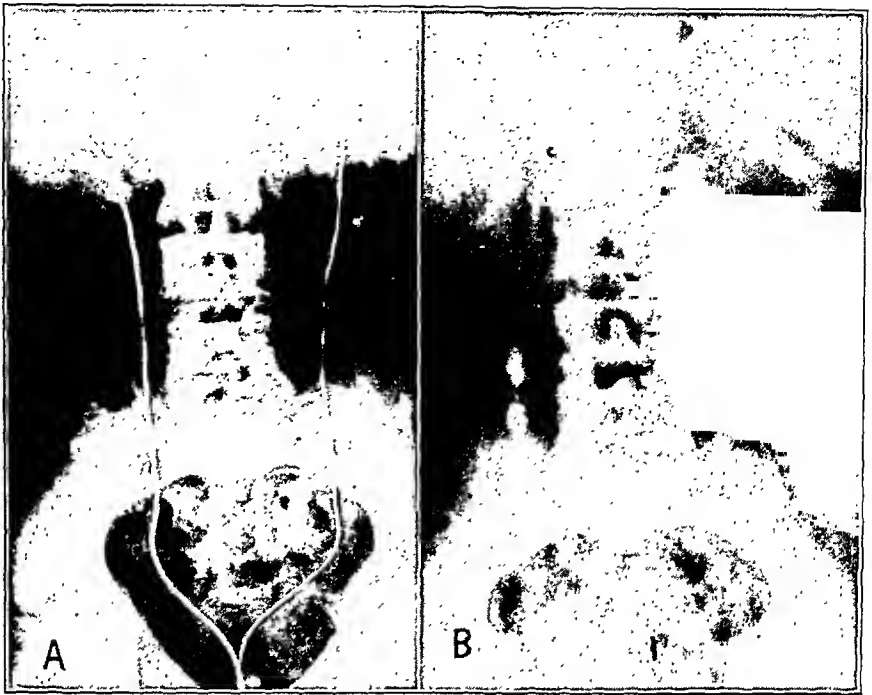


Fig. 22.—Hyperparathyroidism with bilateral nephrolithiasis. Multiple seed calculi are seen in the parenchyma of both kidneys. The impacted calculus in the lower part of the left ureter (*A*) required ureterolithotomy. Later a ureterolithotomy on the right was necessary for two large calculi impacted in the right ureter (*B*).



Fig. 23.—Recurrence of two large calculi (*A*) in the lower part of the right ureter in the case illustrated in figure 22, a few months later. Perforation occurred followed by perinephric abscess, generalized peritonitis and death. Osteoporosis characteristic of hyperparathyroidism is evident in the bones (*A* and *B*). After the first operation for stone, a parathyroid tumor weighing 10 Gm. was removed from the patient's neck. The calcium and phosphorus content of the blood remained abnormal. Two more parathyroid adenomas were found at autopsy.

attempts to promote passage of the stones were unsuccessful, and the patient's general condition rendered surgical intervention exceedingly precarious. The ureter was perforated by the stone (perhaps aided by cystoscopic manipulation), and the patient died. Autopsy revealed a perinephritic abscess and general peritonitis with abscess of the spleen, while further examination of the neck revealed one large and one small parathyroid adenoma, which had been missed when the first adenoma was removed. This accounted for the failure of the calcium and phosphorus content of the blood to return to normal.

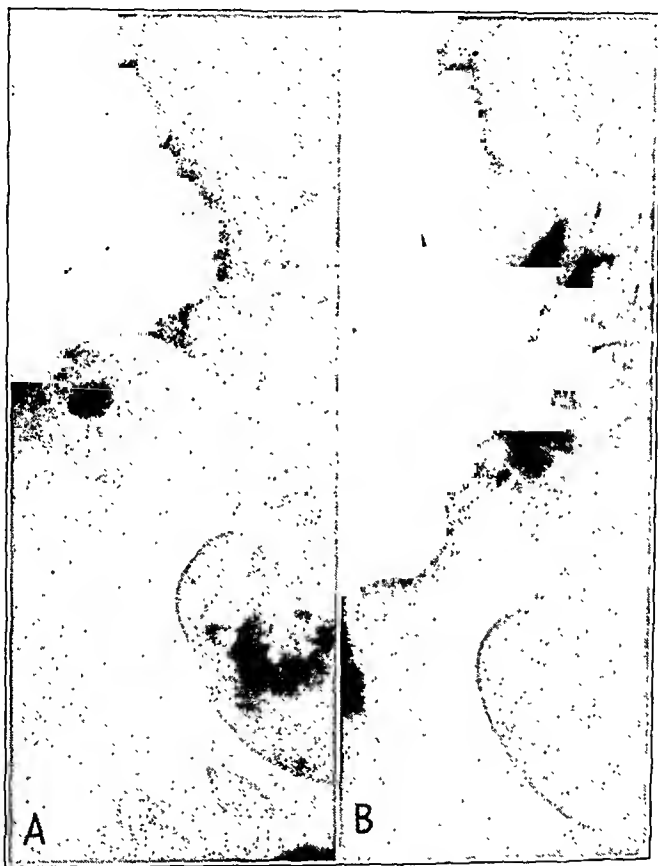


Fig. 24.—Large impacted stone in the right ureter, causing hydronephrosis: *A*, plain roentgenogram of kidney, ureter and bladder; *B*, pyeloureterogram. Ureterolithotomy on the right and appendectomy were performed at the same time through a McBurney incision.

COINCIDENT URETEROLITHOTOMY AND APPENDECTOMY

Figure 24 illustrates the case of a woman of 25, who had more or less discomfort for several years in the right lower quadrant of the abdomen.

During all this time it was taken for granted that she had chronic appendicitis, until urologic investigation revealed a large stone in the lower part of the right ureter. Since cystoscopic removal was obviously out of the question, uretero-

lithotomy through a lateral incision was done without delay. Through the same incision the peritoneum was opened and a normal appendix removed. The patient was convinced that her appendix was at fault, and there seemed to be no valid objection to combining the two operations. In figure 24 the kidney appears to be badly damaged, yet its functional restoration was perfect after removal of the stone.

TOTAL DESTRUCTION OF ONE KIDNEY WITH CALCULOUS PYONEPHROSIS: ANURIA AFFECTING THE NORMAL MATE

Figures 25 and 26 illustrate the case of a woman 45 years of age who exhibited complete destruction of the right kidney by calculous pyonephrosis.

A complete urologic investigation showed the opposite kidney to be normal in every respect. Following cystoscopy, anuria occurred and could not be overcome by any of the usual means. A second cystoscopy was done, and a catheter could not be passed up the left ureter, although it had passed easily at the first cystoscopy. After six days of total anuria, pyelotomy was performed on the left. The pelvis and ureter were distended with urine which gushed forth freely. Retrograde catheterization of the left ureter was done. The wound healed promptly, and normal urination was reestablished. The nature of the obstruction in the left ureter causing the anuria still remains a mystery. The patient would not submit to further treatment and was discharged from the hospital. In spite of the presence of a large calculous pyonephrosis she enjoyed fair health for four years. Severe pain then developed in her right side, with chills and fever, and she was persuaded to come back to the hospital, where nephrectomy was performed on the right, with a successful outcome.

PROBLEMS OF STONE IN CONNECTION WITH RENAL TUBERCULOSIS

Calcification is demonstrable by roentgenography in from 10 to 20 per cent of cases of renal tuberculosis. However, the combination of stone and renal tuberculosis is comparatively uncommon.

Figure 27 illustrates a case of renal tuberculosis associated with stone in the lower part of the ureter.

The surgical problem was whether to do the usual nephrectomy or a nephroureterectomy. A simple nephrectomy was done, with an excellent result. The patient has been followed closely for five years since operation, and the stone in the stump of the tuberculous ureter has never caused the least trouble.

Figure 28 illustrates a case of tuberculosis of the left kidney with stone in the pelvis of the right kidney.

The patient, aged 30, had Potts' disease as a child. Nine years previously I had performed bilateral epididymectomy for tuberculosis. Two years before he had had an active pulmonary lesion, which became quiescent after a year in an Arizona sanatorium. Since it was thought best to preserve the integrity of his right kidney, pyelolithotomy was done on the right. One year has passed since that operation, but so far, because the tuberculous left kidney is silent and he has no symptoms of disorder in the bladder, he has refused nephrectomy.



Fig. 25.—Calculous pyonephrosis (right) and normal left kidney. The bilateral pyelogram (*A*) shows the stone in the right kidney, but the pyelographic medium fills only the lower part of the ureter, where an S-shaped strictured area is seen. The stricture probably resulted from complications associated with difficult labor. In *B* is shown a pyeloureterogram of the same kidney partially filled with sodium iodide. Nephrectomy on the right was planned, but after cystoscopy the patient had anuria for six days owing to blockage of unknown cause in the lower part of the left ureter. Pylotomy on the left and retrograde catheterization of the left ureter overcame the anuria (fig. 26).



Fig. 26.—Intravenous urogram in the case illustrated in figure 25, four years later. Note the deformity on the left resulting from the previous operation to cure anuria. Nephrectomy was now performed on the right and the large calculous pyonephrosis removed. During the previous four years the patient had been free from symptoms, but she came for operation because of an attack of pain in the right side associated with chills and fever and acute perinephric involvement.



Fig. 27.—Stone remaining in a tuberculous left ureter six years after nephrectomy for tuberculosis of the left kidney. The patient is well and free from symptoms.



Fig. 28.—Plain roentgenogram of kidney, ureter and bladder in a case with old Pott's disease, tuberculosis of the left kidney and calculus in the right renal pelvis. Pycelolithotomy was performed on the right.

CONFUSION OF EXTRARENAL SHADOWS. WITH RENAL STONE

Usually no difficulty is found in determining whether a given concretion is in the urinary tract or extraurinary, but occasionally special procedures are necessary to settle this point. The stereogram with ureteral catheter in place is often helpful, or a lateral exposure, as in the case illustrated in figure 29, will definitely determine this point.

SPONTANEOUS DISAPPEARANCE OF LARGE RENAL CALCULUS

The case illustrated in figures 30 and 31 is reported as a curiosity without any attempt at explanation.

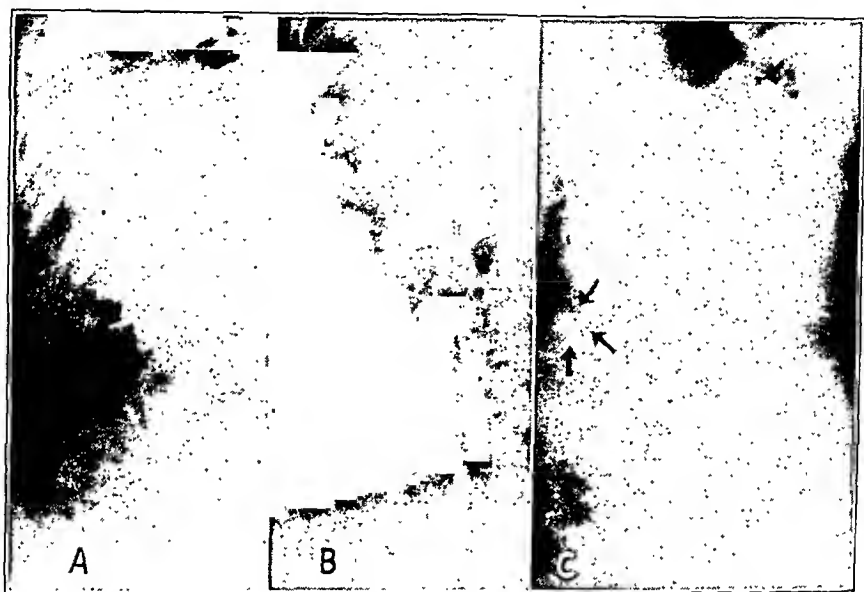


Fig. 29.—Renal colic on the right, associated with infected hydronephrosis: *A*, plain roentgenogram of kidney, ureter and bladder, showing the stone, which in the pyelogram (*B*) appears to be situated in the upper major calyx. The lateral view (*C*) proves that this is a gallstone because of its anterior position. A renal stone would be in the same plane as the spine.

The patient, a man 48 years of age, came to the Southern Pacific Hospital suffering with renal colic. Urologic investigation revealed large bilateral renal calculi of the staghorn type associated with chronic pyelonephritis (fig. 30). Since function was most impaired on the right, a nephrolithotomy was done on that side. The patient was then sent home to recuperate, with instructions to return within a month for operation on the left kidney. He did not return for four years. Investigation then showed (fig. 31) that the large staghorn calculus in the left kidney had apparently disappeared spontaneously. His pyuria had likewise cleared up, and there was no evidence of recurrence on the right side. During these



Fig. 30.—Bilateral renal calculi of the staghorn type: *A*, plain roentgenogram of kidney, ureter and bladder; *B*, bilateral pyelogram. Nephrolithotomy was performed on the right (fig. 31).

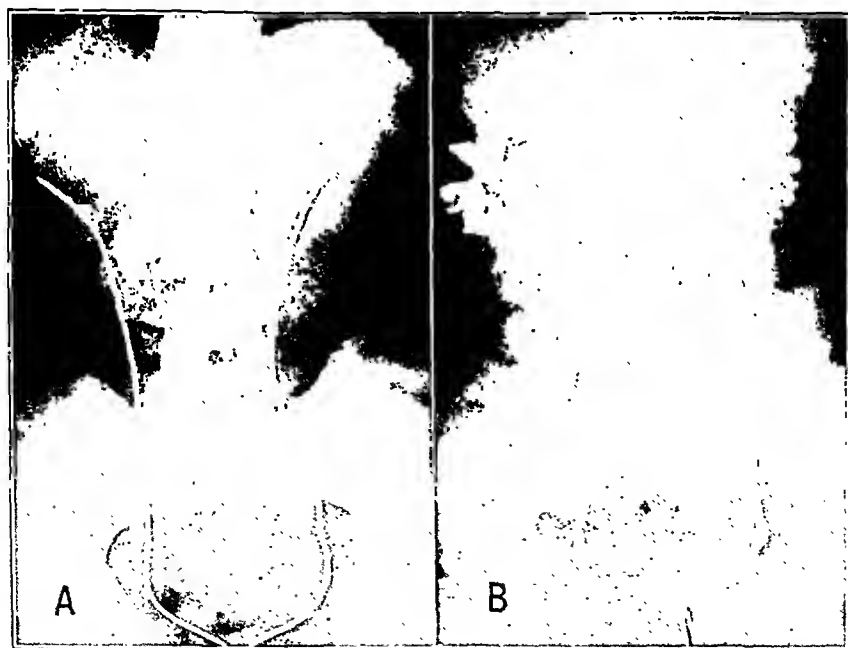


Fig. 31.—*A*, plain roentgenogram of kidney, ureter and bladder; *B*, bilateral pyeloureterogram in the case illustrated in figure 30 four years after nephrolithotomy on the right. Note that the large staghorn calculus in the left kidney has apparently disappeared spontaneously.

four years the patient had been under no dietary regimen or treatment of any kind. On his own initiative he had for one year drunk a daily cup of tea brewed from horsetail grass.¹

CASE OF UNUSUALLY LARGE CALCULOUS PYONEPHROSIS

In calculous pyonephrosis the kidney usually increases in size, but never in my personal experience has one assumed as extensive proportions as that shown in figure 32.

It will be noted that the diaphragm on the right side is markedly raised and that the shadow of the kidney extends from the ninth rib above to the pelvic brim below. The patient was a man, aged 52, who gave a history of occasional discomfort in his right side and periodic hematuria but engaged actively in business. He did not seek medical attention until struck in the back by an

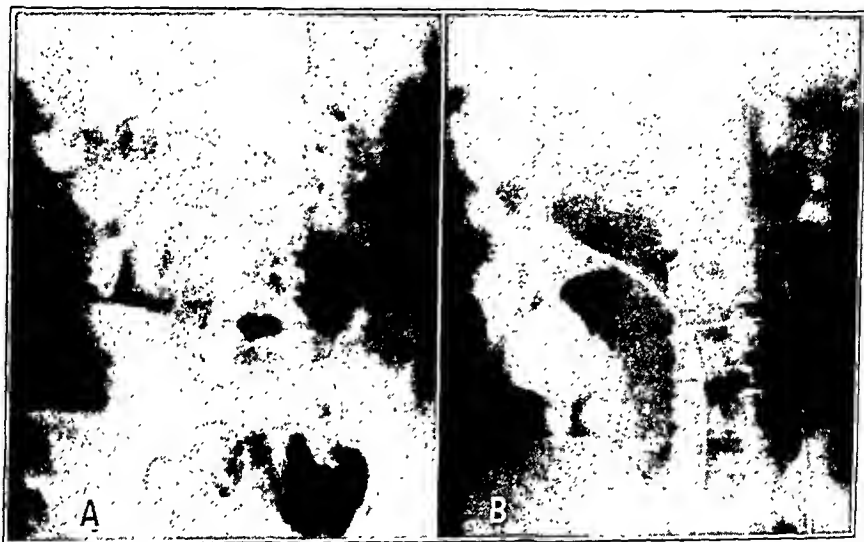


Fig. 32.—Unusually large calculous pyonephrosis: *A*, plain roentgenogram of kidney, ureter and bladder; *B*, pyelogram with incomplete filling. Note that the shadow of the kidney extends from the ninth rib above down to the pelvic brim. The patient was struck in the back by an automobile, and gross hemorrhage from this kidney resulted. An emergency nephrectomy was done to prevent fatal hemorrhage.

automobile. The accident started gross hematuria, and an emergency nephrectomy was necessary to prevent fatal hemorrhage.

SUMMARY

A series of experiences are related dealing with some of the problems encountered in the surgical treatment of renal calculi.

1. A communication from the Council on Pharmacy of the American Medical Association relative to horsetail grass ascribed to it no therapeutic value beyond a mild diuretic action.

An hydraulic maneuver of value in the removal of the small, elusive renal calculus is described.

The value of the ureteral splint and its use after pyelotomy and ureterotomy are described.

Cases are cited illustrating (*a*) choice between nephrotomy, heminephrectomy and nephrectomy, (*b*) problems in the management of bilateral calculi, (*c*) cystoscopic versus operative management of ureteral stone, (*d*) gas gangrene of the wound following operation for renal stone with comment on treatment by serum and roentgen rays, (*e*) hyperparathyroidism as an etiologic factor in the formation of renal calculi, (*f*) coincident ureterolithotomy and appendectomy, (*g*) calculous pyonephrosis with anuria involving the opposite normal kidney, (*h*) phases of stone associated with renal tuberculosis, (*i*) extrarenal shadows confused with renal calculus, (*j*) spontaneous disappearance of large renal calculus and (*k*) calculous pyonephrosis of unusual proportions.

450 Sutter Street.

COMPLETE EXCISION OF THE CERVICAL GLANDS FOR REGIONAL METASTASES

L. CLARENCE COHN, M.D.

BALTIMORE

Complete excision of the glands of the neck for malignant disease consists of excision of the submental lymphatic glands; unilateral excision of the submaxillary lymphatic and salivary glands and of the occipital, the deep cervical, the paratracheal, the prelaryngeal, the superior anterior cervical, and the infrahyoid lymphatic glands, and resection of the sternocleidomastoid and the omohyoid muscle, and of the internal jugular vein (fig. 1). Descriptions of the operation by Crile and others¹ are in the literature. Each operator's technic naturally is a little different, and, as others have noted, many complete block dissections of the glands of the neck are such in name only; therefore, even at the risk of repetition, it seems well to describe mine.

The position of the patient on the operating table is flat on the back with the neck extended. The incision in the skin extends from the mastoid process of the temporal bone to a point about 2.5 cm. below the angle of the lower jaw and from this point continues parallel to the jaw to a point on the opposite side below the mental foramen. A second incision, beginning at the middle of the clavicle, meets the horizontal incision at a point midway between the angle and the symphysis of the lower jaw (fig. 1). Three flaps are raised by continuing the incision through the platysma myoides muscle and undercutting. At this time it is well to ligate, preferably with fine black silk, the small vessels which have been previously clamped. After the flaps composed of skin, subcutaneous fat and the platysma myoides muscle have been dissected back, the sternocleidomastoid muscle

1. Crile, G.: Excision of Cancer of the Head and Neck with Special Reference to the Plan of Dissection Based on One Hundred and Thirty-Two Operations, *J. A. M. A.* **47**:1780 (Dec. 1) 1906. Horsley, J. S.: Operations for Malignant Tumors of the Neck, *Virginia M. Semi-Monthly* **19**:81, 1914. Quick, D.: Radium and Surgery in Cancer of the Tongue, *Brit. M. J.* **2**:944, 1930. Birkett, G. E.: Radium Treatment of Buccal Carcinoma, *ibid.* **2**:944, 1930. Fraser, J.: Carcinoma of the Mouth and Tongue, *Tr. Am. S. A.* **50**:8, 1932. Myers, E. S., and Duhig, J. V.: Surgery and Pathology of Cancer of the Head and Neck, *J. Cancer Research Com., Univ. Sydney* **5**:30, 1933. Blair, V. P., and Brown, J. B.: The Treatment of Cancerous or Potentially Cancerous Cervical Lymph Nodes, *Ann. Surg.* **98**:650, 1933. Fischell, E.: Unilateral Block Resection of the Lymph Nodes of the Neck for Carcinoma, *Am. J. Surg.* **30**:27, 1935. Quick, D.: Metastatic Epidermoid Carcinoma of the Neck: Technical Considerations in the Combined Method of Treatment, *ibid.* **30**:207, 1935. Crile, G., and Kearns, J. E., Jr.: Branchial Carcinoma: Lateral Cervical Neoplasm, *Surg., Gynec. & Obst.* **60**:703, 1935.

is divided a short distance above the clavicle, the external jugular vein first being divided and ligated. The division of the sternocleidomastoid muscle brings into view the omohyoid muscle, which is in turn divided at the level of the division of the sternocleidomastoid. The internal jugular vein is now visible and readily accessible. The sheath of the vein is divided, and a section of the vein 4 cm. in length is mobilized. A ligature of double zero chromic catgut is placed around the vein with an aneurysm needle. A second ligature, of fine black silk, is placed just above the catgut. Both ligatures are tied, and the vein is doubly clamped above the second tied ligature and divided between the clamps, the upper clamp

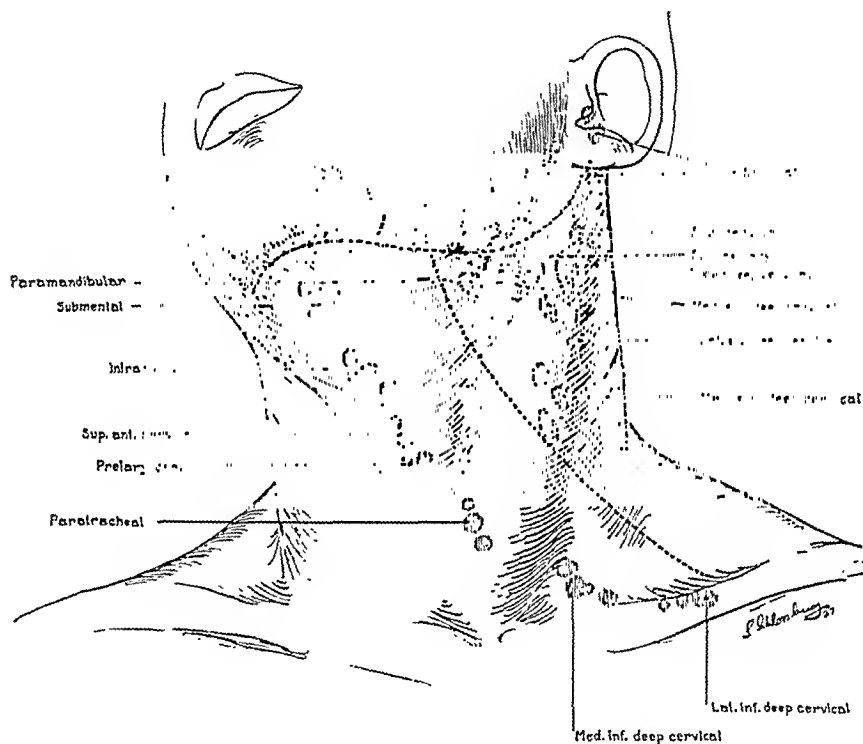


Fig. 1.—Distribution of the superficial and the deep lymphatic glands of the neck. The interrupted lines indicate the incisions in the skin.

being left in situ. I have always transfixed a third ligature to the distal stump of the vein, using a straight intestinal needle threaded with fine black silk (fig. 2).

The common carotid artery is then exposed quickly by dividing the carotid sheath (fig. 3). The carotid sheath is stripped upward, the bifurcation of the carotid artery thus being brought into view. Rather than to attempt ligation of the branches of the external carotid artery at this stage it is preferable to continue the excision along the anterior margin of the omohyoid muscle as far as the hyoid bone, clamping, dividing and ligating the superior thyroid vessels as they come into view, at the same time excising the lymphatic area anteriorly as far as the sternohyoid and the thyrohyoid muscle, removing the paratracheal, prelaryngeal, superior anterior cervical and infrahyoid lymphatic glands. The omohyoid muscle is then excised near the hyoid bone.

Next is the excision of the submental lymphatic glands, and in order to make this complete it is well to expose the periosteum of the lower jaw and to carry the excision of glands to the capsule of the submaxillary salivary gland on the opposite side. When the primary carcinoma is situated on the anterior third or the tip of the tongue or on the lower lip, it is well to study a frozen section of the lymphatic gland between the opposite submaxillary gland and the jaw, as metastasis to this gland indicates bilateral involvement. The endotherm needle

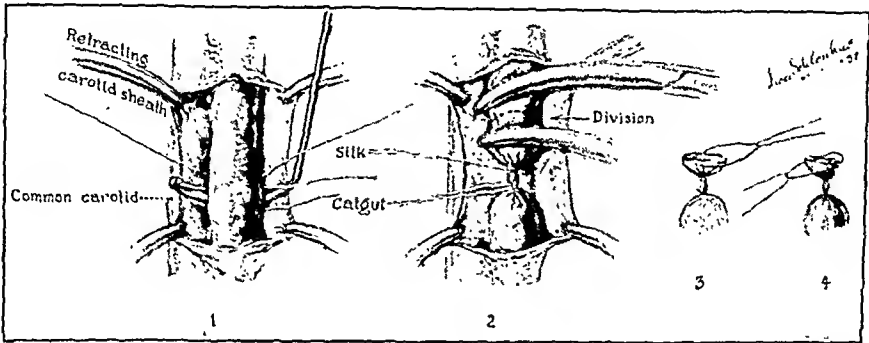


Fig. 2.—Mobilization, ligation and division of the left internal jugular vein in the lower third of the neck.

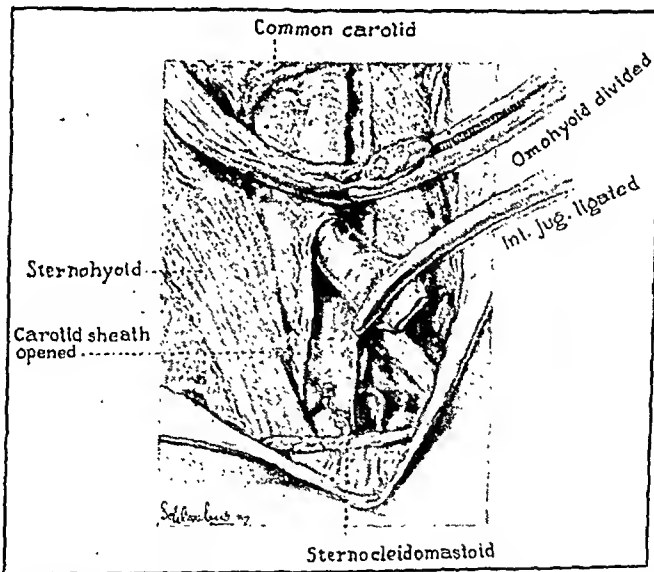


Fig. 3.—Ligation and division of the internal jugular vein completed.

may be used for the greater part of the dissection and especially for excising the submental glands and for the dissection along the lower jaw.

The facial vein and the external maxillary artery are ligated and divided, and by retraction on the mylohyoid muscle the submaxillary salivary and the sublingual glands are readily excised up to the mucous membrane of the floor of the mouth. The submental and the submaxillary glands are gently rotated posteriorly, the bifurcation of the carotid artery being thus again exposed. The branches of the external carotid artery are divided between clamps and ligated. When the primary

carcinoma involves the base or middle third of the tongue, the lymphatic glands near the bifurcation of the carotid artery are sometimes extensively involved and adherent to the carotid sheath. Even so, it is rarely necessary to ligate the external carotid artery. To facilitate the excision of this deep group of cervical glands it is often advisable to excise or divide the posterior belly of the digastric muscle.

The next procedure is the ligation and division of the artery and the vein to the parotid gland and the division of the sternocleidomastoid muscle near the mastoid process. The upper deep cervical and the occipital glands are then accessible and are removed up to the base of the skull. The internal jugular vein is clamped and ligated a short distance below the jugular foramen. It is usually safer to use an electric cautery in excising the occipital and the superior cervical

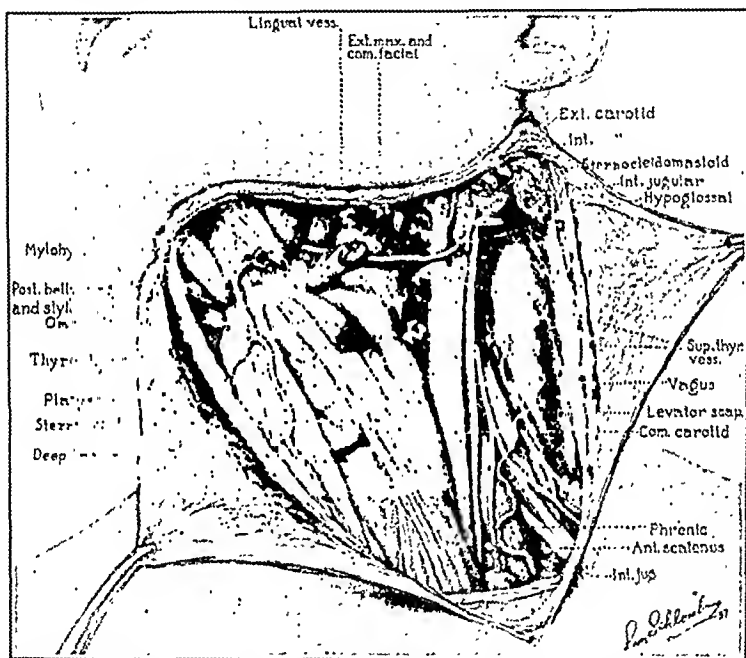


Fig. 4.—Wound after the complete block dissection of the cervical glands, showing the extent of the surgical excision.

glands if they appear grossly involved. The excision of glands is continued distally from this point, and the deep cervical glands behind the excised internal jugular vein are included in the excision. At this time procaine hydrochloride is injected into the neural branches to the scalenus muscles and the levator scapulae muscle, and the supraclavicular glands (median and lateral inferior deep cervical) are excised to the junction of the internal jugular and the subclavian vein and posteriorly and laterally to the scalenus muscles (fig. 4). The clamps controlling the small bleeding points are quickly ligated; sometimes a triangular area of skin is excised where the two incisions meet, and the wound is rapidly closed to within 2 cm. of the clavicle by approximating the skin with interrupted sutures of fine black silk. Although there is considerable serosanguineous drainage for about twenty-four hours, primary healing occurs almost without exception (fig. 5).

The credit for the conception of the mechanism of the surgical pathologic anatomy of cervical glands which are the seat of metastases from carcinoma of the head and neck belongs to Crile. Disregarding conventional methods of incomplete excision of the cervical glands for carcinoma, he conceived, employed and established on a rational basis the surgical excision of these glands. Applying the knowledge of Halsted's method of axillary dissection to the excision of the cervical glands in 1898, only four years after Halsted's first description of his operation, he reported in 1906 the results of 36 radical block dissections of the cervical glands. Crile did more than apply Halsted's method to the neck. He recognized that the *sine qua non*, or, as he expressed it, the "key to the situation," is the complete excision of the internal jugular vein.



Fig. 5.—Photograph of a patient taken June 7, 1935, two years and seven months after complete excision of the cervical glands. The patient was well Sept. 11, 1937, four years and ten months after the operation. The primary lesion was a carcinoma of the tip of the tongue.

Judging from the relatively small number of papers on this subject during the thirty-one years since Crile's contribution and from personal observation and conversation with colleagues, I believe that there is a lack of enthusiasm for the operation on the part of physicians except among the small number particularly interested in this domain. In the succeeding pages facts will be presented in the hope of proving that this skepticism is not entirely warranted. Even among the workers in this field there is a difference of opinion as to whether the operation should be done as a routine whenever the primary lesion is malignant or only after evidence of metastases. It has been my practice to subject to this operation only patients in whom there was definite metastasis or presumptive evidence of metastasis confirmed by a study of a frozen section at the beginning of the complete excision.

The etiologic factors, the methods of prevention and early recognition and the treatment of the original tumor, although of prime importance, are not considered in this study. Also excluded from consideration are cases in which the operation was of less extent and those in which there was a block resection of the tongue, the floor of the mouth, the lower jaw and the glands of the neck in one stage, because the problems involved are somewhat different. A restricted operation on the cervical glands is often adequate for carcinoma of the lower lip. On the other hand, in cases of advanced carcinoma of the tongue the floor of the mouth and mucous membrane of the lower jaw or the jaw itself as well as the regional lymphatic glands may be involved. The additional extent of the involvement and the lowered resistance of the patient in such cases carry a larger operative mortality. There is, moreover, a much higher

TABLE 1.—*Metastatic Carcinoma of the Cervical Glands: Diagnosis of the Primary Lesion*

	No. of Cases
Carcinoma of the tongue	16
Carcinoma of the mucous membrane of the cheek.....	3
Carcinoma of the lower lip	3
Carcinoma of the mucous membrane of the lower jaw.....	1
Carcinoma of the mucous membrane of the antrum of the upper jaw.....	1
Carcinoma of the brachial cleft	3
Malignant pigmented mole.....	3
Carcinoma in lateral aberrant thyroid tissue.....	1

percentage of recurrence during the immediately succeeding and later years. I have largely given up this radical operation in cases in which the condition is advanced.

This study is confined to the consideration of cases of operable carcinoma in which there was secondary involvement of the cervical glands by metastases from a primary lesion located in the region of these glands. There were 31 cases, in all of which I operated between the years 1925 and 1937. In each instance one or more of the glands were palpable at the examination before the operation and the presence of cancer confirmed in the microscopic sections later. In table 1 are noted the diagnoses of the primary tumor in the 31 cases. Carcinoma of the tongue was present in approximately 50 per cent; carcinoma of the mucous membrane of the cheek, carcinoma of the lower lip, carcinoma of the branchial cleft and malignant pigmented moles, 10 per cent in each, and carcinoma of the mucous membrane of the antrum, carcinoma of the mucous membrane of the lower jaw or carcinoma in lateral aberrant thyroid tissue, in the remaining 10 per cent. No patient with regional metastasis from carcinoma of the larynx is recorded in this table, because such patients have not been considered suitable subjects for the operation in question.

The operative mortality in this series of 31 cases was approximately 10 per cent. Of the 3 deaths, 2 were from pneumonia, lobar pneumonia on the seventh day and bronchopneumonia on the ninth day; and 1 patient died at the end of twenty-four hours with symptoms suggesting embolism. This operative mortality of 10 per cent is far too high, and it can, I am confident, be materially reduced. In 21 of the 31 cases the operation was performed with local anesthesia (procaine hydrochloride), and in these 21 cases the operative mortality was nil. Three of the 10 patients given general anesthesia died, a mortality of 33.3 per cent among these patients. After the first death from bronchopneumonia, on the ninth day after ether drop anesthesia, in January 1926, general anesthesia was not used for more than four years. In August 1930 an operation was performed with avertin anesthesia, and death occurred in twenty-four hours with symptoms suggesting embolism. In June 1933, after anesthesia induced with avertin and ether given by rectum, bronchopneumonia developed, and the patient died of this disease in one week. Since that time (June 1933), the operations have been done with local anesthesia. I am convinced in view of this record that operations with general anesthesia involve too large a mortality to be risked, and without hesitation I recommend that the operation be done with local anesthesia if it is at all possible. The time required for this operation is about three hours, and general anesthesia for this length of time, in conjunction with this type of surgical intervention, contributes materially to postoperative complications.

After the 3 cases of postoperative death are deducted, there remain 28 cases in which the end results may be considered. Of the 16 cases in which the glands were the seat of metastatic carcinoma primary in the tongue, 13 fell within this 28. The primary tumor was located at the tip or along the lateral margin of the tongue in 13 cases and at the base in 3. In 12 of the 13 cases the tumor histologically was a low grade spinal cell carcinoma with marked differentiation toward adult epithelium and contained many pearly bodies (fig. 6). In 1 case the sections and tissue have been lost. In the 3 cases in which the primary carcinoma was at the base of the tongue the tumor histologically was a highly malignant undifferentiated transitional cell carcinoma without formation of pearly bodies. Of the 13 patients who survived the operation, 8 (61 per cent) have been alive and well for periods varying from a few months to almost eleven years (table 2). Only 1 of these 8 had the primary carcinoma on the base of the tongue (fig. 7).

Each of the 3 metastatic carcinomas of the cervical glands primary in the mucous membrane of the cheek histologically was a low grade well differentiated spinal cell carcinoma with formation of pearly bodies. All 3 patients remained well more than five years. Two of them are still well ten and a half and six years respectively after operation; 1 died

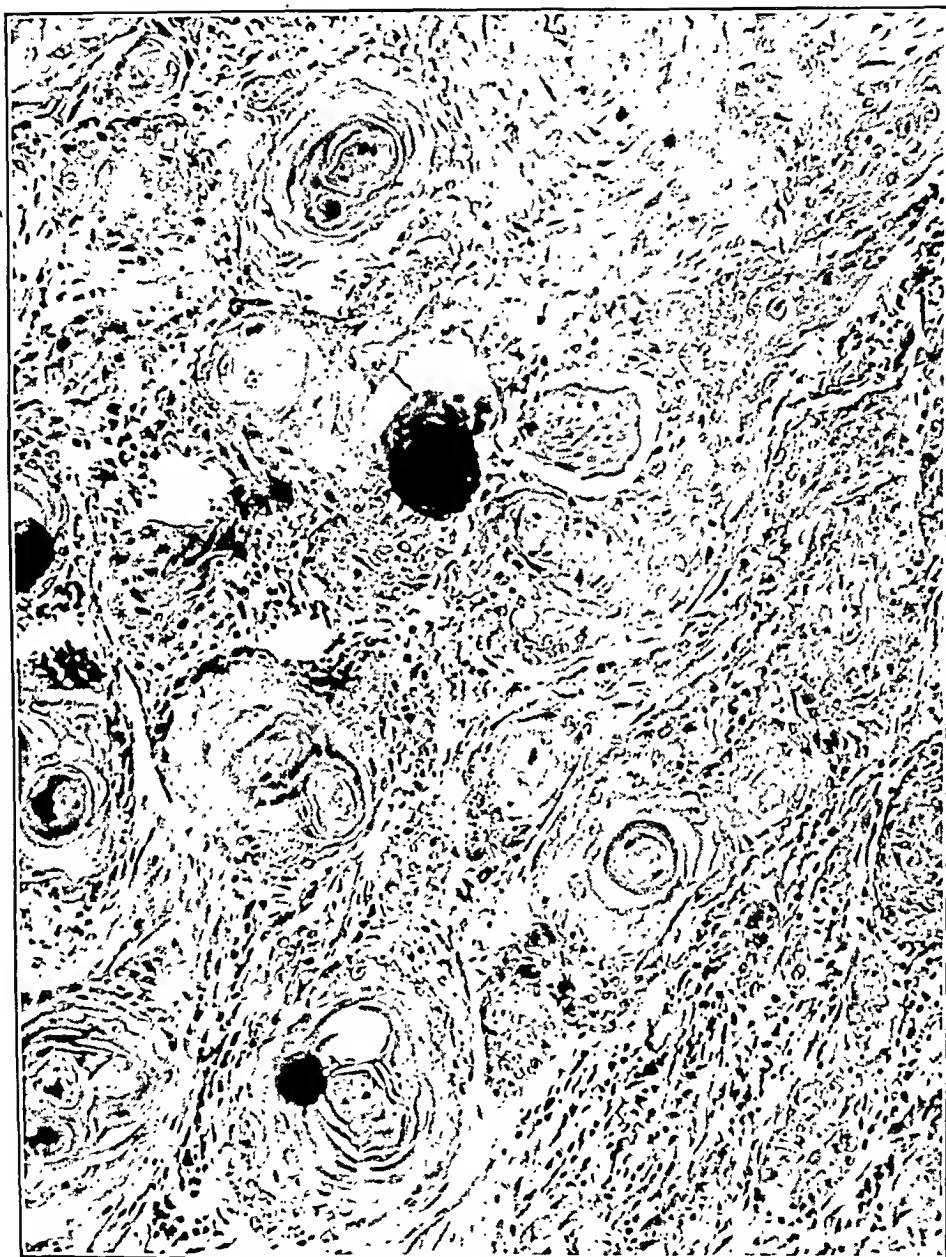


Fig. 6.—Low power photomicrograph of a cervical lymphatic gland, showing low grade spinal cell carcinoma with many pearly bodies. The complete excision of the cervical glands took place on Nov. 9, 1926. The patient was well July 10, 1937. The primary carcinoma involved the lateral margin of the middle third of the tongue.



Fig. 7.—Low power photomicrograph of a cervical lymphatic gland, showing transitional cell carcinoma which characteristically occurs at the base of the tongue. In the case here illustrated there were two courses of preoperative irradiation followed by the complete excision of the cervical glands on Oct. 3, 1935. The patient was well on June 16, 1937.

eight years and five months after operation, and the autopsy revealed no evidence of recurrence or metastases (fig. 8; table 3). The complete operation was performed only 3 times for carcinoma primary in the lower lip. Two of the patients died of cancer within a few months of the operation. In 1 case, in which the histologic grading was III, involvement of the pharynx was found at operation, and in the other, in which the histologic grading was IV, the lowest supraclavicular gland was the seat of metastasis. The third patient is well and free from

TABLE 2.—*Metastatic Carcinoma of the Cervical Glands from Carcinoma of the Tongue (16 Cases)*

	No. of Cases
Postoperative death.....	3
Death of cancer.....	4
Duration of life after excision of glands: 4 mo., 5 mo., 7 mo., 1 yr. 3 mo.	
Death of pneumonia 4 days after excision of cancer of the tongue.....	1
(Cervical glands excised by previous operation)	
Patients living and well July 15, 1937.....	8
Duration of life since excision of glands:	
Under 1 yr.....	1
2 to 3 yr.....	4
4 to 5 yr.....	1
7 to 8 yr.....	1
11 to 12 yr.....	1

TABLE 3.—*Metastatic Carcinoma of the Cervical Glands from Carcinoma of the Mucous Membrane of the Cheek (3 Cases)*

	No. of Cases
Patient living and well 10½ yr. after operation.....	1
Patient living and well 6 yr. after operation.....	1
Death 8 yr. and 5 mo. after operation; autopsy revealed no evidence of cancer	1

TABLE 4.—*Metastatic Carcinoma of the Cervical Glands from Carcinoma of the Lower Lip (3 Cases)*

	No. of Cases
Death of cancer within a few months after operation.....	2
Patient living and well 3 yr. after excision of glands.....	1

recurrence three years after operation, even though the glands were extensively involved by metastases, and in spite of the fact that there had been a previous incomplete operation on the neck in another clinic. Histologically this tumor was graded II (table 4).

There was 1 case of carcinoma primary in the mucous membrane of the antrum of the upper jaw and 1 of carcinoma primary in the mucous membrane of the lower jaw. Histologically these tumors were graded II and III respectively. Both patients died of cancer within six months of the operation. Likewise in the 3 cases of carcinoma primary in the

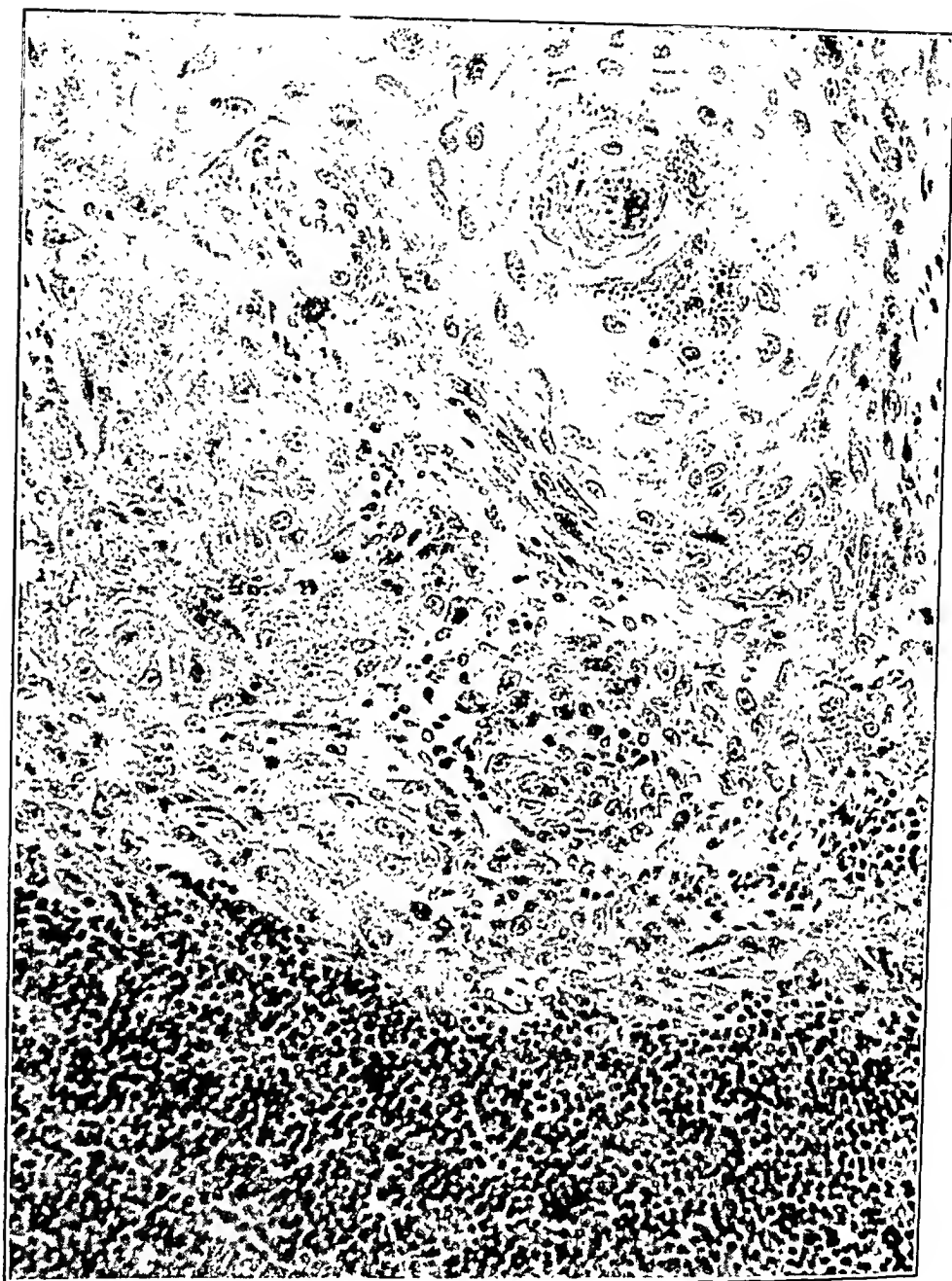


Fig. 8.—Low power photomicrograph of a cervical lymphatic gland, showing low grade spinal cell carcinoma. Complete excision of the cervical glands was done on Dec. 4, 1928. The patient died on May 9, 1937. The autopsy revealed no evidence of carcinoma. The primary carcinoma involved the mucous membrane of the cheek.

branchial cleft and in the 3 cases of metastases to cervical glands from malignant pigmented moles the termination was fatal (figs. 9 and 10). The histologic grading in the 3 cases of carcinoma of the branchial cleft was III, IV and IV, respectively (fig. 11). Tables 5 and 6 give the duration of life after operation. There is 1 patient living and well two years and eight months after the complete excision of the cervical glands for metastatic carcinoma primary in lateral aberrant thyroid tissue (figs. 12 and 13).

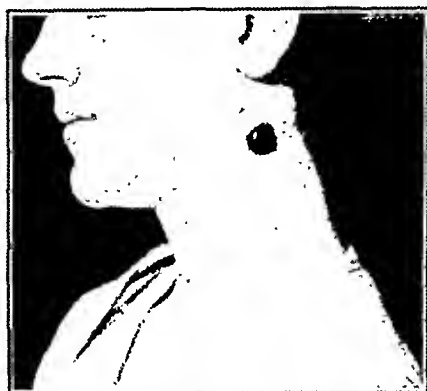


Fig. 9.—Photograph of a patient who had a malignant pigmented mole of the skin of the neck with extensive metastasis to the cervical glands. Preoperative interstitial radium therapy was given. Complete excision of the mole and the cervical glands was done on Jan. 6, 1933. The patient died on Oct. 30, 1933, from metastasis.

TABLE 5.—*Metastatic Carcinoma of the Cervical Glands from Carcinoma of the Branchial Cleft (3 Cases)*

Death of cancer 7 mo. after operation
Death of cancer 1 yr. 2 mo. after operation
Death of cancer 3 mo. after operation

TABLE 6.—*Metastatic Carcinoma of the Cervical Glands from a Malignant Pigmented Mole (3 Cases)*

Death of cancer 2 yr. 2 mo. after operation
Death of cancer 1 yr. 4 mo. after operation
Death of cancer 10 mo. after operation

Just what part irradiation ultimately will take in the handling of these cases is difficult to establish at this time. In table 8 is a summary of the irradiation therapy employed in this series. From the study of this relatively small group of cases in which the primary lesion and consequently the metastatic glands represent a number of different patho-



Fig. 10.—Low power photomicrograph of a cervical lymphatic gland, the seat of metastasis from a malignant pigmented mole of the skin of the neck. Pre-operative external roentgen irradiation was employed. Complete excision of the tumor and the cervical glands was done on Jan. 5, 1933. The patient died in May, 1934, of metastasis to the brain.

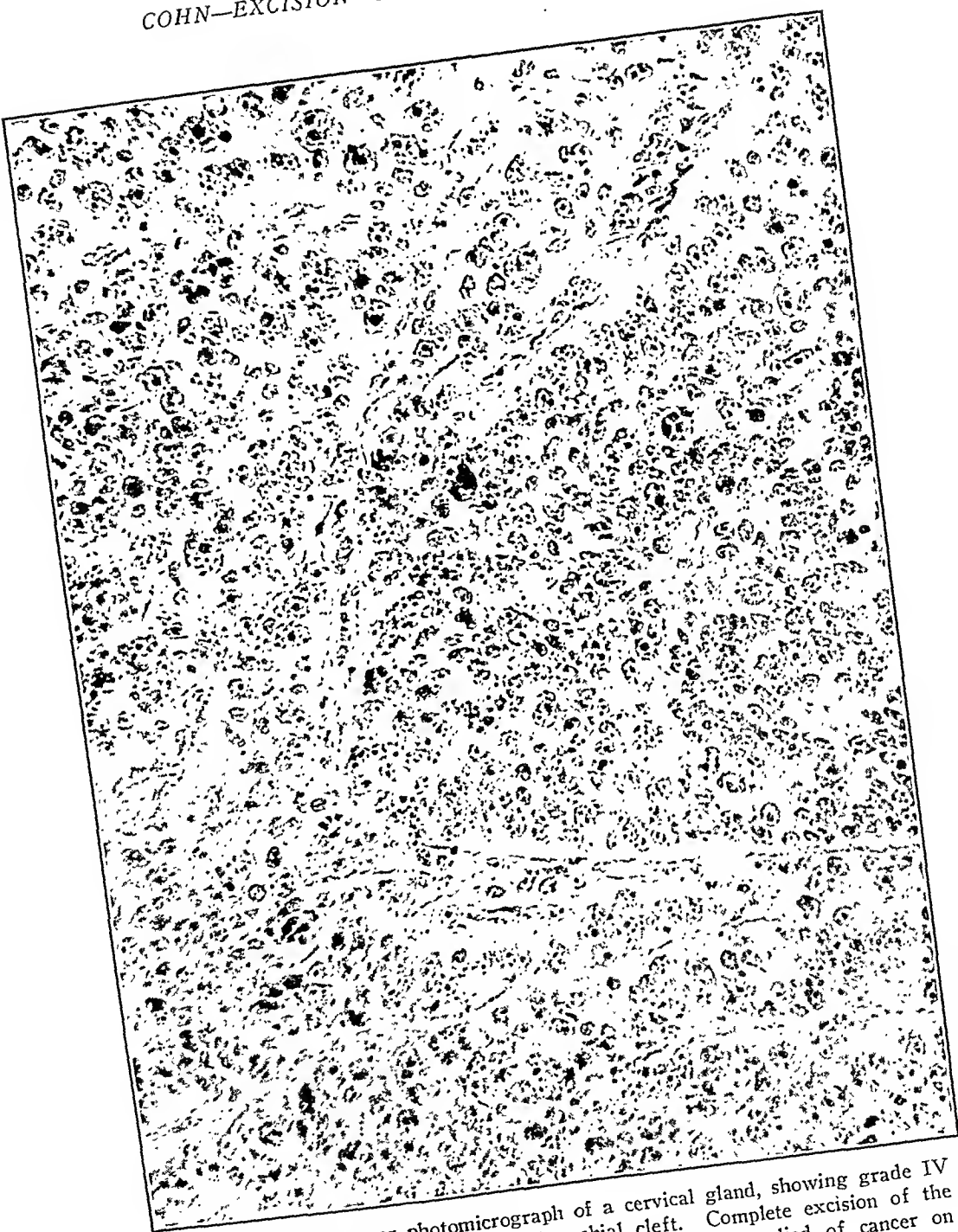


Fig. 11.—Low power photomicrograph of a cervical gland, showing grade IV spinal cell carcinoma primary in the branchial cleft. Complete excision of the cervical glands was done on Aug. 10, 1925. The patient died of cancer on Oct. 11, 1926.

TABLE 7.—*Metastatic Carcinoma of the Cervical Glands*

	No. of Cases
Primary lesion in the mucous membrane of the upper jaw.....	1
Death of cancer 4 mo. after operation	
Primary lesion in the mucous membrane of the lower jaw.....	1
Death of cancer a few months after operation	
Primary lesion carcinoma in lateral aberrant thyroid tissue.....	1
Patient well 2 yr. 8 mo. after operation	

TABLE 8.—*Metastatic Carcinoma of the Cervical Glands: Therapy by Irradiation*

	No. of Cases
A. Primary lesion in the tongue—16 cases	
Preoperative irradiation (roentgen) of the cervical glands.....	8
Well 1 to 2½ yr. after operation.....	4
Death of cancer 2	
(5 mo. after operation; 1 yr. 3 mo. after operation)	
Postoperative death 2	
Postoperative irradiation (roentgen) of the cervical glands.....	2
Well 7½ yr. after operation.....	1
Death 3½ mo. after operation.....	1
Postoperative irradiation (radium) of the cervical gland on the opposite side (Patient well 4 yr. 10 mo. after operation)	1
No irradiation 5	
Patient well 2	
(11 yr. 6 mo. after operation; 2½ mo. after operation)	
Death 3	
(7 days after operation of pneumonia; 5 days after excision of cancer of the tongue, of pneumonia; 7 months after operation, of cancer)	
B. Primary lesion in the mucous membrane of the cheek—3 cases	
No irradiation 3	
Patient well 2	
(8 yr. 9 mo. after operation; 6 yr. after operation)	
Death 1	
(8 yr. 5 mo. after operation; autopsy revealed no evidence of recur- rence or metastasis)	
C. Primary lesion in the lower lip—3 cases	
Preoperative irradiation (roentgen).....	1
(Patient well 3 yr. after operation)	
No irradiation 2	
(Death a few months after operation; death 4 mo. after operation)	
D. Primary lesion in the branchial cleft—3 cases	
Preoperative irradiation (roentgen).....	1
(Death 4 mo. after operation)	
No irradiation 2	
(Death 1 yr. 5 mo. after operation; death 7 mo. after operation)	
E. Primary lesion malignant pigmented mole—3 cases	
Preoperative irradiation (radium).....	2
(Death 9 mo. after operation; death 1 yr. 4 mo. after operation)	
Postoperative irradiation (roentgen).....	1
(Death 2 yr. 2 mo. after operation)	
F. Primary lesion in other locations—3 cases	
Primary lesion in the mucous membrane of the upper jaw.....	1
No irradiation	
(Death 4 mo. after operation)	
Primary lesion in the mucous membrane of the lower jaw.....	1
Postoperative irradiation (roentgen)	
(Death a few months after operation)	
Primary lesion carcinoma in lateral aberrant thyroid tissue.....	1
Preoperative irradiation (radium)	
(Patient living and well 2 yr. 8 mo. after operation)	

logic processes, only a few conclusions seem justified. While it is impossible without producing irreparable damage to deliver by external irradiation a lethal dose of roentgen rays or radium to any but a very ray-sensitive tumor, there seems to be no danger in delaying the operation for a course of preoperative irradiation when the glands are not palpable, or for the purpose of testing the sensitivity of the tumor to rays when they are palpable. In 13 instances, because of metastases or because the microscopic picture was such as to suggest the probability of metastases, the glands were irradiated and then excised or excised later when they became palpable.



Fig. 12.—Photograph of a patient on Nov. 5, 1934, showing a tumor in the submaxillary area of the neck. The scar on the lower lip is from the excision of a benign wart fifteen years before. There was preoperative radium treatment. The cervical glands were completely excised on Nov. 22, 1934. The patient was well on July 9, 1937. For the microscopic appearance of the tumor, see figure 13.

Occasionally after irradiation there was a diminution in the size of the palpable gland or glands, but in only 2 instances was there complete disappearance of a metastatic cervical gland under irradiation, and in 1 of these there was no conclusive evidence that the gland was actually cancer. In the other a gland that was the seat of metastasis from carcinoma of the base of the tongue disappeared completely after a course of external irradiation but recurred in six months. A second course of irradiation was given without any change in the size of the gland, and after the second course of irradiation the glands were completely excised (fig. 7). In the former, a case in which there was no preoperative irradiation, a nodule developed over the right side of the larynx four months after a complete operation on the left side. In a few days this



Fig. 13.—Low power photomicrograph of a cervical lymphatic gland, showing papillary adenocarcinoma primary in lateral aberrant thyroid tissue. Figure 12 shows a photograph of the patient before operation.



Fig. 14.—Low power photomicrograph of the capsule of a cervical lymphatic gland, showing residual carcinoma. There were two courses of preoperative roentgen irradiation. The cervical glands were completely excised on Jan. 3, 1935. The patient was well on April 5, 1937. The primary carcinoma involved the middle third of the tongue.

nodule reached 2.5 cm. in diameter and appeared as though it were going to burst. Two radon seeds were introduced into the mass, after which the lesion, apparently carcinoma, rapidly disappeared and has not recurred during the four years and four months since the irradiation (fig. 5).

In some instances there were distinct changes in the microscopic pathologic condition of the glands in cases of low grade well differentiated carcinoma with pearly bodies, which in all likelihood were due to the irradiation. Granting that cervical glands that are sites of metastases from carcinoma of the tongue sometimes undergo extensive necrosis and cystic degeneration, I have never observed in the non-irradiated gland the changes which occurred after irradiation in 1 of these cases. In this instance the gland resembled an atheromatous cyst, with a capsule like the wall of a cyst and with contents soft and cheese-like. The only evidence of residual carcinoma histologically consisted of a few nests of squamous cells firmly confined in a much thickened capsule, although the cystic mass was about 4 cm. in diameter (fig. 14).

CONCLUSION

Enough time has elapsed since operation in a sufficient number of cases to allow the statement that many patients who had carcinoma of the cervical glands are now well. Had they not been subjected to the complete excision of these glands, with or without irradiation, they would not be living and free from recurrence. This fact is ample evidence to warrant the conclusion that this type of surgical intervention, alone or combined with irradiation, offers sufficient hope for the cure of patients with regional metastases from carcinoma in the cervical glands to justify its adoption in all cases in which the condition is operable.

PSEUDOULCERS OF THE DUODENUM OF THE NORMAL DOG

INCLUDING A STUDY OF THE INCIDENCE OF INTESTINAL
ULCERS IN THE NORMAL DOG

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Considerable work has been done on the production of ulcers in the intestinal tract of the dog. The incidence of experimentally produced ulcers varies with the type of operative procedure employed. The Exalto and the Mann Williamson technic give the highest percentages of positive results. A detailed description of these methods was given in a previous report. The relative immunity of the duodenum to formation of ulcer by experimental methods is therein commented on.

The existence of ulcers in the gastrointestinal tract of the normal laboratory animal which has not been operated on is of rare occurrence; no particular attention is called to this in the literature. We determined, therefore, to make observations of the entire gastrointestinal tracts of apparently normal dogs and to determine the incidence of intestinal ulcers in these animals.

We have recently reported work from this laboratory on the production of experimental duodenal ulcers in the dog and have called attention to the occurrence of circular punched-out depressions in the duodenum, which at first glance appear to be ulcers. It seems that little or no attention has been paid to these findings by the various investigators doing experimental work with the gastrointestinal tract of the dog. This is noteworthy because such depressions may easily on gross inspection be erroneously diagnosed and may have been mistaken for ulcers by workers in this field.

It is not our object to go into elaborate detail as to the normal anatomic and histologic picture of the duodenum of the dog. Our attention was confined to these ulcer-like depressions which are especially abundant in the duodenum and which are apparently a usual finding. We wished also to determine the incidence of ulcer in the intestinal tract of the normal dog which has not undergone an opera-

tion. There is no reference in the clinical literature¹ (so far as it has been available to us) to these pseudoulcerous depressions.

Chauveau^{1a} and more recently Bradley² in their descriptions of the duodenum of the dog made no mention of such depressions. Sisson³ in his book "The Anatomy of Domestic Animals," in describing the intestinal tract of the dog, stated:

Aggregated lymph nodules or Peyer's Patches are numerous (about 20 in number in young subjects) and begin in the duodenum. They are usually elliptical in outline and the last one is band-like and reaches the end of the ileum and is four to sixteen inches long.

In describing the histologic picture of the intestinal tract of man, Jordan⁴ stated:

Above the level of the ileum the largest collection of lymph tissue in the intestinal mucosa occurs in the duodenum where there are extensive infiltrations of dense lymphoid tissue, many of which contain typical nodules with germinal centers. These masses of lymphoid tissue are penetrated by the ducts of duodenal glands whose secretion forms a bed upon which the lymphoid tissue rests. The duodenal "patches" differ slightly from those in the ileum in that they form a more confluent mass with relatively few nodules. They also possess a more diffuse character, are more deeply situated and are therefore covered by the corium of the mucosa which contains both intestinal glands and villi.

MATERIALS AND METHODS

The animals used in this study were taken from among those used in the department of physiology for experimental purposes. They had not been subjected to any type of experimentation that might in any manner affect the gastrointestinal tract. They were taken at random, irrespective of age, weight or breed; only those animals that appeared healthy, however, were used. These animals were killed and the entire gastrointestinal tract was removed and was examined as follows:

1. Observation of the entire gastrointestinal tract in situ was made.
2. The entire tract was opened and the gross appearance and internal structure observed with the following points especially in mind:
 - a. Number, size, location and appearance of ulcers, if any;
 - b. Number, size, location and appearance of depressions, or pseudoulcers.

1. Ochsner, A. J.: Further Observations on the Anatomy of Duodenum, *Am. J. M. Sc.* **132**:1, 1906.

1a. Chauveau, A.: *Comparative Anatomy of the Domesticated Animals*, London, J. & A. Churchill, 1891.

2. Bradley, O. C.: *Topographical Anatomy of the Dog*, New York, The Macmillan Company, 1935.

3. Sisson, S.: *Anatomy of Domestic Animals*, Philadelphia, W. B. Saunders Company, 1921.

4. Jordan, H. E.: *Textbook of Histology*, ed. 6, New York, D. Appleton-Century Company, Inc., 1934.

3. Photographs of the depressions in the gross specimen were taken. Microscopic sections of the depressions were also made.

4. Photographs of the gross specimen and microscopic sections of the Peyer patches in the ileum were made.

ANATOMIC FINDINGS

We have examined the entire gastrointestinal tracts of over 75 dogs without finding evidence of ulcers in any. The animals were all apparently healthy except that 10 had worms. Only 55 of the dogs, however, have been considered in this study. The type record for findings with data is shown below:

Date 4/22/37

Dog 10 Breed—Collie Wt.—18 Kg. Sex—Female

Appearance—Healthy; slight conjunctivitis

Miscellaneous information—Killed with ether

Stomach—No ulcers

Duodenum:

Gross external appearance—Nine raised circular pale patches measuring 3 to 12 mm. in diameter, along the antimesenteric border

Gross internal appearance—Depressed area corresponding to those seen externally, arranged in linear alinement

Depressed areas—Total number, 9; size, 3 to 10 mm. in diameter; location, antimesenteric border mostly; appearance, circular; punched-out; rolled edges; base covered with normal mucosa

Ulcers—Total number, none; size, none; location, none; description, none

Jejunum

Depressed areas—Total number, 2; size, 2 to 4 mm. in diameter; location proximal

Antimesenteric border—Circular; punched-out; covered with normal mucosa

Ulcers—None

Ileum

Depressions—None

Ulcers—None

Colon

Depressions—None

Ulcers—None

Microscopic Section—Depression in mid-duodenum; section made; stained with hematoxylin and eosin

For the 55 animals studied there was no evidence of ulcers in the stomach, the duodenum or the small or the large intestine. There were noted, however, in the duodenum, circular punched-out depressions along the mucosal surface, measuring from 3 to 15 mm. in diameter and varying in number from three to ten. These depressions corresponded for the most part with similar raised circular areas seen on the serosal surface of the duodenum, which were paler than the surrounding

mucosa. The bile and pancreatic ducts usually opened into the duodenum about $\frac{3}{4}$ to $1\frac{1}{2}$ inches (2 to 4 cm.) from the pylorus.

These depressions were entirely confined to the duodenum; in young animals, however, they were also seen in the proximal part of the jejunum. In 1 subject about 6 weeks old the depressions in the duode-

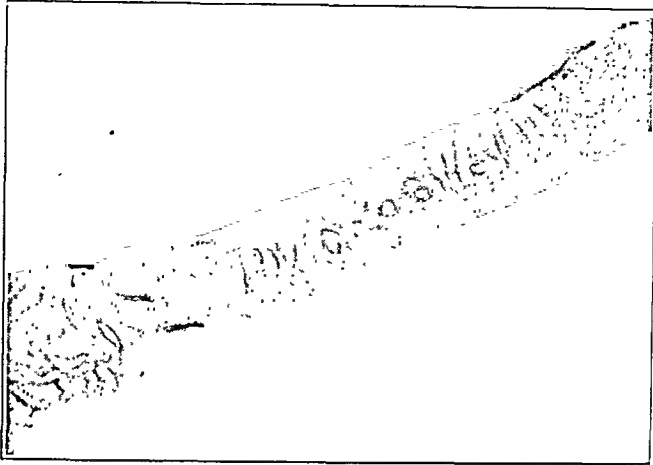


Fig. 1.—Photograph of the duodenum of a normal dog. Note the circular punched-out depressions in linear arrangement. These closely resemble ulcers.

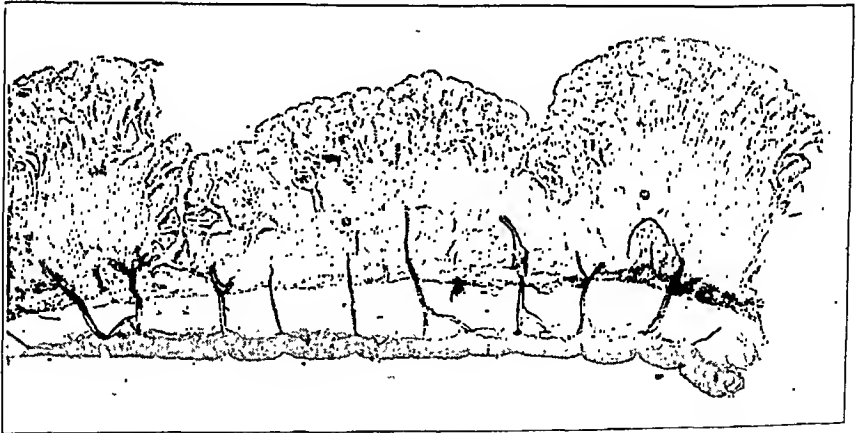


Fig. 2.—Section from the upper part of the duodenum of a normal dog, showing punched-out depressions. Note the thinness of the mucosa at this site and also the absence of the crypts of Lieberkühn. There is some lymphocytic infiltration of the submucosa and the tunica propria. Note the tendency toward reduplication of the muscularis mucosae and the submucosa at the periphery of the depression.

num were numerous and were present even down to the proximal part of the ileum. The depressions gradually became more shallow from the duodenum to the ileum, until they became raised above the mucosal surface as true Peyer patches, as seen in the lower portion of the ileum.

These depressions as they were seen grossly along the mucosal surface of the duodenum appeared much like punched-out ulcers, but on close inspection it was noted that the edges were not undermined but were rather rolled and smooth and that the base and the entire surface were covered with normal intact mucosa. The depressions did not correspond to the valvulae conniventes seen in the human duodenum;

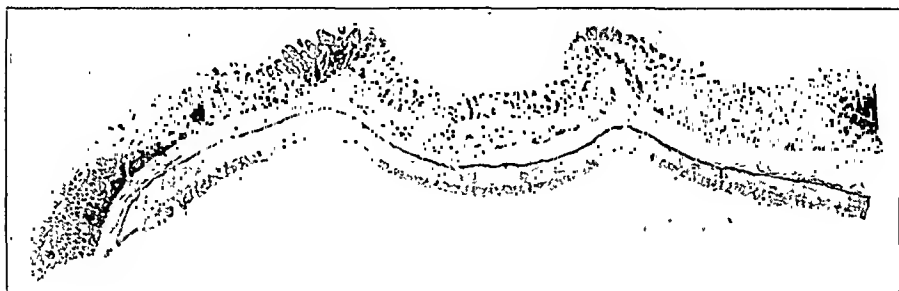


Fig. 3.—Section through the lower part of the duodenum, showing another depression. This does not show the marked thinness of the mucosa at the site of the depression as does figure 2. It does, however, show the out-pouching of the serosa at this site and also the reduplication of the muscularis mucosae and the submucosa at the periphery of the depression. Note also the three small areas of lymphocytic aggregation in the submucosa.

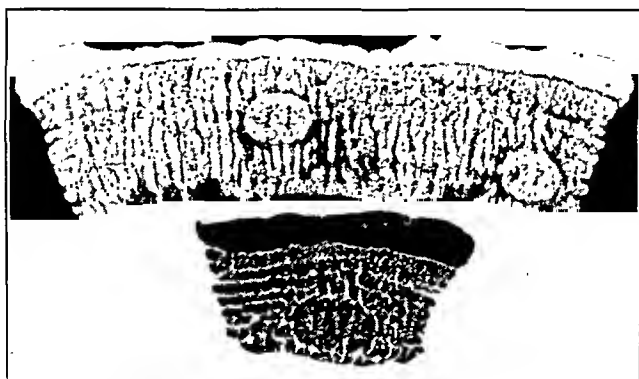


Fig. 4.—Lower third of the ileum of a normal dog, showing typical Peyer patches. Compare this with figure 1, which shows depressions of the duodenum.

in fact, true valvulae conniventes were not observed at all in the dog. Five per cent of the duodenums showed smooth mucosa grossly. The depressions were present in 50 of the 55 dogs considered or 90.8 per cent.

Figure 1 is a photograph showing the duodenal mucosa of a normal animal which has not been operated on. Note the punched-out depressions in linear arrangement. At first glance they appear to be ulcers.

Figure 2 is a low power photomicrograph of a section through one of these depressions, stained with hematoxylin and eosin. This section is taken through the upper third of the duodenum and shows the thickness of the wall and the absence of Brunner glands at this particular

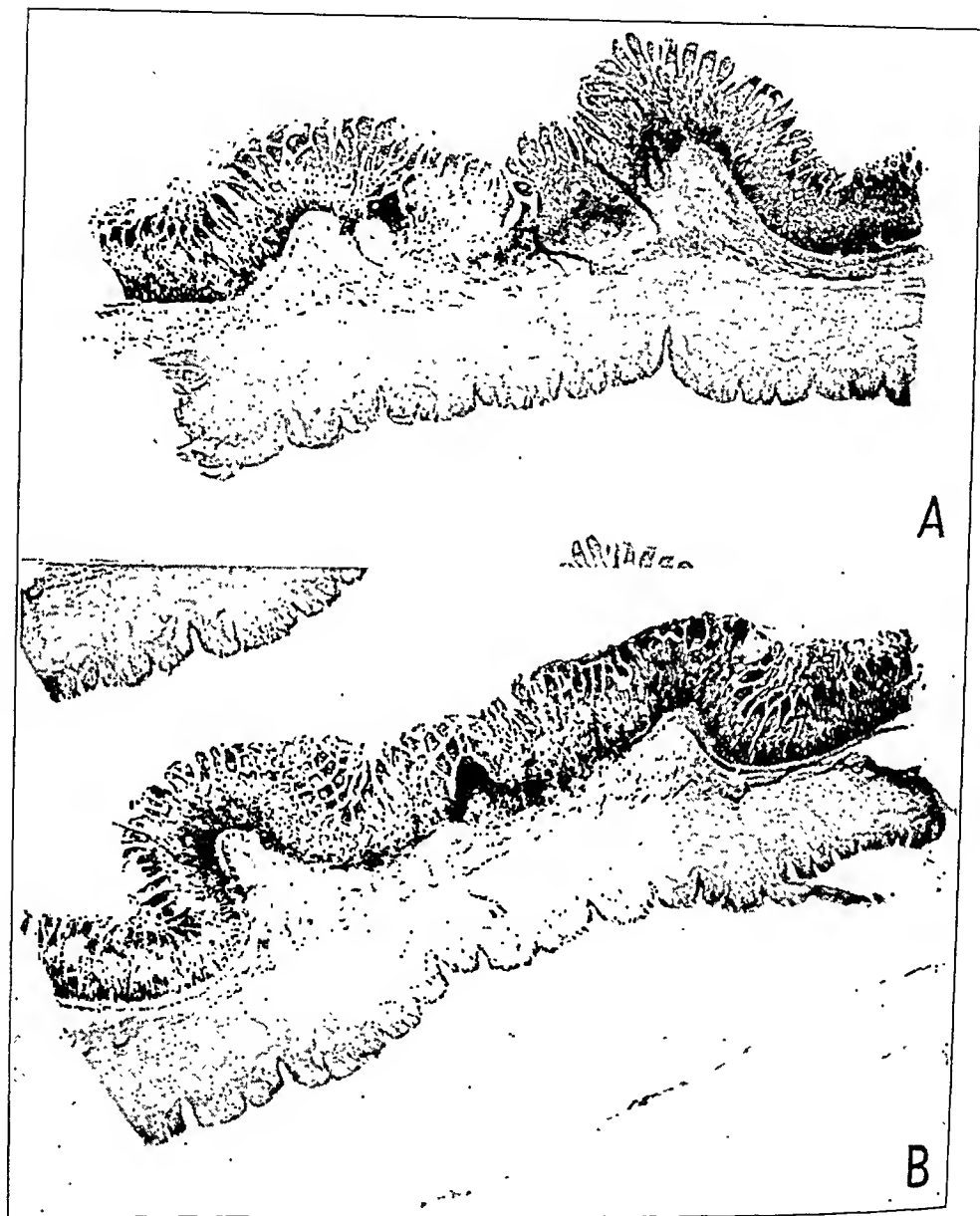


Fig. 5.—*A*, section through a Peyer patch removed from the lower part of the ileum of a normal dog. Note the presence of the lymph nodules with typical germinal centers, the uniform thickness of the mucosa throughout and the projection of the mucosa at this site into the lumen of the bowel. *B*, another section through a Peyer patch removed from the lower part of the ileum of a normal dog. Compare with figure 5 *A* above.

level. Brunner glands in the duodenum of the dog are present only for a very short distance from the pylorus. The mucosa in this region is intact throughout the entire section despite the definite depression. The depression is due to a thinning out of the mucosa at this site. The crypts of Lieberkühn beneath the depression are shallow or appear to be lacking entirely. The submucosa and the corium of the tunica propria showed some lymphocytic infiltration, with a few small nodules. The lymphocytic infiltration is not dense or diffuse like that seen in a typical Peyer patch. There is in this section a tendency for reduplication of the submucosa and the muscularis mucosae, but the muscular and serosal coats are not disturbed.

Figure 3 shows a section through a depression removed from the duodenum of another animal, taken through the lower third. This section is practically identical with the one seen in figure 1. In this



Fig. 6.—Microscopic section through an ulcer from the middle third of the duodenum. Note the absence of Brunner glands at this level.

section, however, the depression and reduplication are more marked, and there is a definite out-pouching of the serosal coat. It is to be noted that although there is some lymphocytic aggregation it does not seem to be very marked. Many sections revealed absence of any form of lymphocytic cell accumulation. We should say, however, that these areas may correspond to, but are not identical with, the Peyer patches. The depressions certainly do not show marked lymphocytic aggregation in the mucosa and submucosa with eversion of the mucosa and projection of the "path" into the lumen of the bowel, as does a typical Peyer patch.

Figure 4 is a gross photograph of a typical Peyer patch, removed from the ileum for comparison. The elevated character of the agminated lymphatic follicles of the Peyer patch is readily appreciated.

In figure 5 the microscopic picture of the Peyer patch illustrates projection into the intestinal lumen, with rich accumulation of lymphatic cells about the germinal centers.



Fig. 7.—Section through the upper part of a normal duodenum close to the pylorus. Note the thickness of the wall, the presence of Brunner glands at this site and the rather scant evidence of lymphocytes.

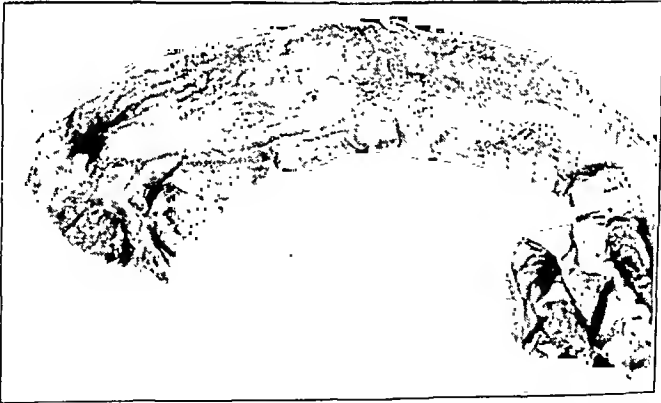


Fig. 8.—Gross photograph showing ulcers in the duodenum, experimentally produced.⁵

Figure 6 shows a duodenal ulcer in microscopic section produced by an operative procedure mentioned elsewhere.⁵ Figure 7 shows a microscopic section of normal duodenum close to the pylorus. Note the presence of Brunner's glands at this site and the rather scant evidence of lymphocytes.

COMMENT

The depressions mentioned were present in most of the animals examined. They were not localized areas of peristalsis, as they might first appear when seen on the serosal surface in the living animal. They were due to a definite out-pouching of the intestinal wall at the site, with a thinning of the mucosa. It is possible, as we have already mentioned,⁵ that such areas may be the site of ulcer formation (experimental) in the duodenum. This, however, we have not been able to prove.

We call attention to this observation because it might prove confusing to one doing experimental work on the gastrointestinal tract. This indicates necessity for microscopic section in the study of suspicious areas before one can definitely determine whether these are ulcers or not.

SUMMARY AND CONCLUSIONS

A study of the gastrointestinal tract of the normal dog is presented; special emphasis is placed on the duodenum. Particular attention is directed to the incidence of ulcers of the intestinal tract in animals used for experimental work. Attention is called also to the occurrence of punched-out depressions on the mucosal lining of the duodenum, which is an apparently normal condition. The following conclusions are offered:

1. No ulcers were found in the intestinal tract of any of the animals studied.
2. The incidence of ulcer-like depressions in the duodenum of the normal dog is 90.8 per cent.
3. These depressions probably correspond to, but are not identical with, Peyer patches.
4. It is possible that these depressions may be confused with ulcers and should be considered as a site of possible ulcer formation by workers attempting to produce experimental ulcers in the dog.
5. Microscopic evidence is necessary before decision is made as to the presence of ulceration.

5. Volini, I. F.; Widenhorn, H. L., and Finlayson, B.: Experimental Duodenal Ulcer, *Surg., Gynec. & Obst.* **65**:159 (Aug.) 1937.

PERIANAL CYSTS OF VESTIGIAL ORIGIN

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The caudal end of the body is a frequent site for the development of cysts, tumors and fistulas of vestigial origin. Here numerous anlagen appear almost simultaneously, some of which proceed through a complex series of changes to form the final organ or system while others develop to a certain stage only to regress and be resorbed. Disturbances in the developmental sequence, arrested development, heterotopia and failure of regression may be factors contributing to the formation of anomalous conditions. The persistence of caudal vestiges and the possibility of their subsequent development into tumors and cysts have been widely acknowledged. These lesions are regarded with much interest not only by the surgeon and the pathologist but also by the embryologist, because of the links which they provide in establishing the chain of evidence concerning the fate of certain embryonal structures.

The present communication will review the embryology of the caudal end of the body in general and the development and regression of anterior sacral and perianal embryonal vestiges formed from a single germ layer in particular. The relation of such vestiges to cysts and tumors of this region will also be discussed. Cases illustrating some of these lesions will be reported.

The human embryo possesses a true tail, which reaches its maximum development at about the 8 mm. stage.¹ From this stage progressive reduction occurs, until the tail has completely disappeared by the time the embryo has grown to about 30 to 35 mm. During this time the several systems which occupy the caudal end of the embryo have appeared and have undergone complex developmental processes. The primitive intestinal tract, the urogenital tract, the early skeletal system, the vascular channels and the neural tube are all involved in the formation of this region.

From the College of Physicians and Surgeons, Columbia University, and the Department of Surgery, the Presbyterian Hospital.

1. Kunitomo, K.: Development and Reduction of the Tail and of the Caudal End of the Spinal Cord, *Contrib. Embryol.* (no. 26) 8:163, 1918.

Early in the development of the embryo (14 to 18 days) a linear ridge, the "primitive streak," appears in the posterior part of the oval embryonic area, which marks the zone of contact of the ectomesodermal vesicle and the entodermal vesicle. This is followed by the appearance of a groove, the "primitive groove," on the surface of the primitive streak. The anterior part of the groove, which extends only about half the distance toward the anterior margin of the embryonic area, terminates in Hensen's node. As the groove develops it forms a perforation which passes through the anterior end of the streak and the underlying entoderm into the entoblastic cavity. This is the blastoporic, or neurenteric, canal (fig. 1 *A*). This communication is highly transitory in man and disappears before the neural groove is converted into a closed tube.

Eternod² described an embryo of 2.1 mm. which showed the beginnings of these structures very well. This was one of the few human embryos in which the neurenteric canal has been observed (fig. 1 *B*).

In this stage, one finds that (1) the neural tube has not yet closed; (2) the notochord and the notochordal canal are present; (3) the neurenteric canal forms a communication between the primitive medullary and intestinal canals; (4) the primitive streak is beginning to form, and (5) the caudal intestine is demarcated by the cloacal membrane.

The medullary tube, which arises by a process of invagination from the neural plate, a derivative of the ectoderm, originally extends the full length of the embryo, including the tail. Before the formation of the medullary tube is complete, however, the neurenteric canal develops just caudad to the terminal portion of the notochord. Presumably the neurenteric canal is composed of tissue derived from both the neural tube and the primitive intestine and should it persist would be found opening caudad to the filum terminale in the coccygeal region.³ The neurenteric canal, however, has never been studied in detail because of its extremely early development and its brief existence. No genuine vestiges or cysts arising from this structure have been described (Peyron⁴).

The caudal end of the neural tube, together with the caudal end of the notochord and the caudal intestine, extends to the ventral side of the tail and fuses with a solid mass of mesodermal cells, forming the so-called "residual mass." At several points the central canal of the neural tube becomes narrowed, and the canal gradually becomes

2. Eternod, A. C. F.: Premiers stades de la circulation sanguine dans l'oeuf et l'embryon humains, *Anat. Anz.* **15**:181, 1898.

3. Lewis, F. T., in Keibel, F., and Mall, F. P.: *Manual of Human Embryology*. Philadelphia, J. B. Lippincott Company, 1912, vol. 2, p. 295.

4. Peyron, A.: Les vestiges embryonnaires de la région sacrococcygienne et leur rôle dans la production des kystes ou tumeurs d'origine congénitale, *Bull. Assoc. franç. p. l'étude du cancer* **17**:613, 1928.

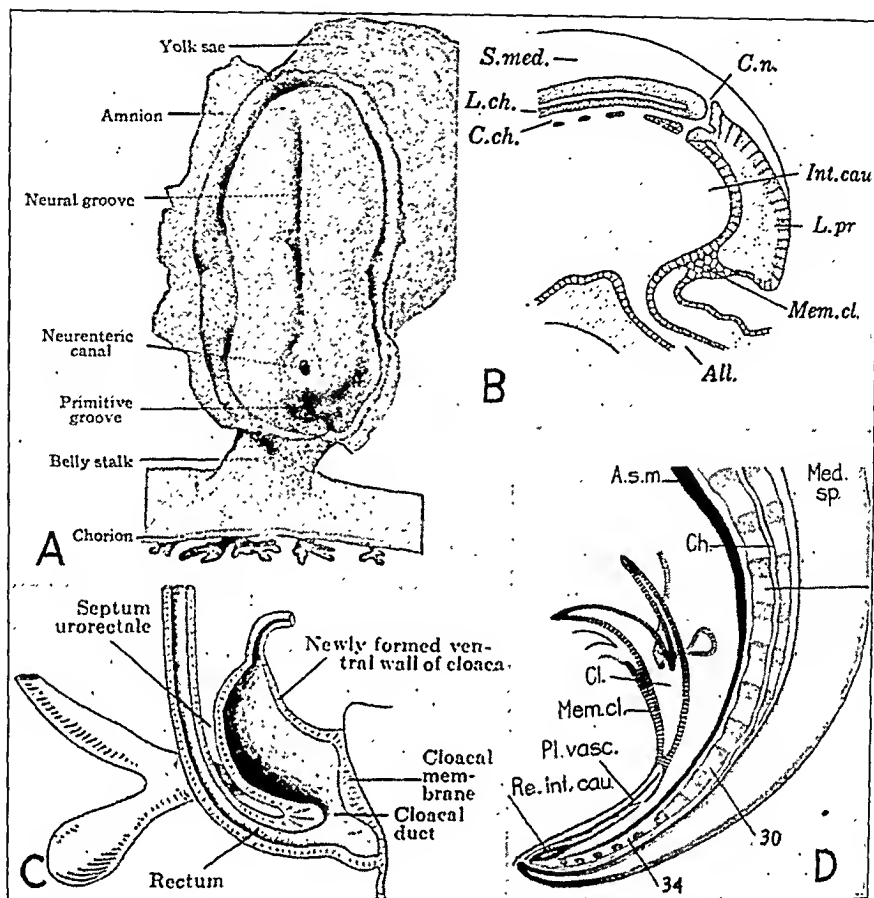


Fig. 1.—A, dorsal view of a human embryo 2 mm. in length, with yolk sac. The amnion is opened dorsally (after von Spee and Kollmann, from Keibal and Mall.³)

B, Eternod's embryo of 2.1 mm. *All.*, allantois; *C. ch.*, chordal canal; *C. n.*, neurenteric canal; *L. ch.*, chordal plate; *L. pr.*, primitive streak; *Mem. cl.*, membrana cloacalis; *S. med.*, medullary groove; *Int. cau.*, intestinum caudale. (From Keibal and Mall.³)

D, embryo of 6.6 mm. The tail has attained nearly its maximum development and will gradually take on a more atrophic appearance. The lines along the dorsal margin of the spinal cord represent the boundaries of the myotomes. Note the beginning separation of the cloaca into dorsal and ventral portions. Note also the isolated caudal gut vestige. *A. s. m.*, arteria sacralis media; *Ch.*, chorda dorsalis; *Med. sp.*, medulla spinalis; *Cl.*, cloaca; *Mem. cl.*, membrana cloacalis; *Pl. vasc.*, plexus vasculosus; *Re. int. cau.*, remnant of caudal gut. (From Kunitomo.¹)

C, embryo of 7 mm. The cloaca is divided into rectum and ventral remains of the cloaca by the urorectal septum. The cloacal duct remains as a communication between the two for a time. (From Keibal and Mall.³)

obliterated, forming a cell strand known as the atrophic cord (fig. 2). At about this time (third month) the relative overgrowth of the vertebral column over the spinal cord occurs, giving the appearance of ascension of the cord in the spinal canal. Remnants of the atrophic cord become dilated and segregated, forming the coccygeal medullary vestige. According to Kunitomo¹ this vestige is usually present and attains its greatest development at the fifth month, forming a white mass about 2 mm. in length in the subcutaneous tissue dorsal to the last coccygeal vertebra. It is composed of tubules which are lined with both stratified squamous and cylindric epithelium, and at birth it has atrophied to a great extent.

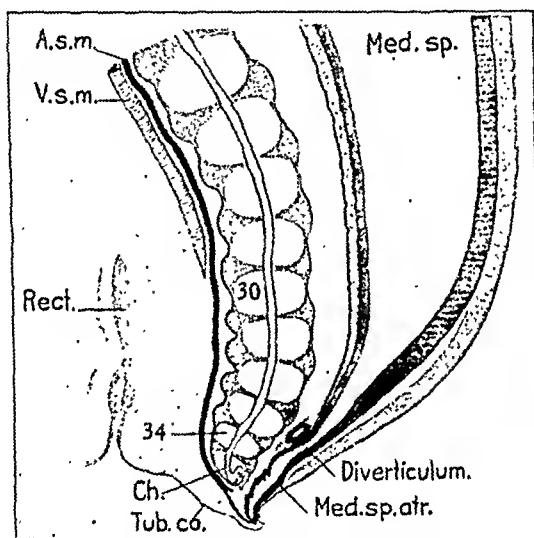


Fig. 2.—Embryo of 25 mm. Note the apparent diverticulum of the atrophic cord. The narrowing of the lumen of this portion of the cord appears to be a characteristic preliminary to its transition into the filum terminale. The two dilations of the terminal intestine are the "bulbus analis" and the "bulbus terminalis." *V. s. m.*, vena sacralis media; *Rect.*, rectum; *Med. sp. atr.*, atrophic portion of spinal cord; *Tub. co.*, coccygeal tubercle. Remainder of abbreviations as noted in figure 1 C. (From Kunitomo.¹)

These vestiges have been thought by some to give rise to pilonidal cysts and sinuses. Recently, Stone⁵ and Fox⁶ have investigated such congenital lesions and have concluded that they develop from centers of growth in the basal layer of the ectoderm, which gives rise to hair follicles and glands. These authors found that such a process of ectodermal invagination is a normal occurrence, and that usually the struc-

5. Stone, H. B.: Pilonidal Sinus, *Ann. Surg.* **79**:410, 1924.

6. Fox, S. L.: The Origin of the Pilonidal Sinus, *Surg., Gynec. & Obst.* **60**:137, 1935.

tures formed disappear. They suggested that it is the same anlage which gives rise to the "preen gland" in certain birds and to analogous structures in certain mammals and reptiles. All of these seem to have a sexual function.

The notochord, which forms the primitive axial skeleton, arises just dorsal to the digestive tube (fig. 1 *B*). Whether it originates from entoderm or from mesoderm has been long debated: Caudal to the termination of the notochord the primitive streak extends to the cloacal membrane, thus passing around from the dorsal to the ventral side.

The evolution of the caudal portion of the notochord is not as well understood as is that of its cranial end. In the period during which the embryo is from 7.5 to 11 mm. in length the greater part of the notochord is embedded in the primitive vertebral column and shows considerable winding.¹ Intervertebral swellings begin to form; fragmentation progresses, and the cartilage of the vertebrae incorporate the vestiges more and more while transforming them. According to Peyron,⁴ the last coccygeal vertebra is formed as a result of fusion of several vertebrae, and this would seem to account for the relative excess of notochordal tissue found in this region.

Vestiges also remain in the region of the spheno-occipital synchondrosis and in the nucleus pulposus of the intervertebral disks. The tissue has a jelly-like appearance and may resemble hyaline cartilage.

The entoderm of the primitive intestinal canal is closed to the exterior for a time but comes into direct relation with the surface ectoderm at the pharyngeal and cloacal membranes. Both of these structures lose their primitive position and become folded into the substance of the embryo through increase in the surrounding mesoderm. The cloacal membrane (figs. 1 *B* and 1 *D*) is formed from the ventral portion of the primitive streak at the time of its displacement in the formation of the tail fold through the disappearance of the intervening mesoderm. The cloacal membrane indicates the division between the terminal portion of the intestine and the tail gut, which normally disappears (fig. 1 *D*). With the development of the wolffian ducts the true cloaca is formed. It represents the common terminal cavity of both the urogenital and the intestinal tract. Subsequently, the separation of the cloaca into a ventral urogenital portion and a dorsal intestinal portion is effected by downgrowth of a coronal urorectal septum (fig. 1 *C*), which is complete at the stage in which the embryo is about 16 mm. in length.⁷ The urorectal septum also divides the cloacal membrane into an anterior urogenital membrane and a posterior anal membrane.

Meanwhile, shrinkage in size does not affect the tail gut evenly throughout its length but is less marked at the caudal extremity, where

7. Johnson, F. P.: Development of the Rectum of the Human Embryo, *Am. J. Anat.* 16:1, 1914.

a cord of cells is found even after all traces of primitive connection with the cloaca have disappeared (fig. 1 *D*). The tail gut is said to appear with the tail and to accompany the tail in its development and resorption.⁸ It appears at about the 3.5 mm. stage, and normally it has completely disappeared in an 8 mm. embryo. Peyron⁴ in an exhaustive study of this structure observed it 10 times in caudates and has presented important data on its histologic and topographic characteristics. He has noted that the early digestive tube is lined with stratified cuboidal epithelium two to four layers thick. The tail gut vestige and the intestinal tube from which it develops are histologically similar. Normally the tail gut vestige fills with epithelial debris and mucus and then rapidly disappears.

At the stage in which the embryo is 13.6 mm. in length the rectum presents a relatively large spindle-shaped swelling, which Johnson⁷ has termed the "bulbus analis" (fig. 2). At the lower end of this swelling the epithelial tube becomes much decreased in size, but just before the cloaca is reached it gradually increases again. The short, lower widened portion has been called the "bulbus terminalis" by the same author. After division of the cloaca and the cloacal membrane into dorsal and ventral portions by the urorectal septum, invagination of the ectoderm of the anal membrane occurs, together with absorption of the intervening mesoderm. A pit is thereby formed, which is termed the proctodeum. Here the ectoderm and entoderm come into contact, and at about the 32 mm. stage perforation of this partition occurs and continuity of the terminal intestinal tract with the ectoderm is established. The junction of the anal and the rectal segment is marked in the adult by the "pectinate," or "white line of Hilton." The bulbus analis forms the lower portion of the ampulla recti in the adult, while the bulbus terminalis forms the zona intermedia of the anorectal canal. In the process of division a portion of the primitive cloaca is included in the bulbus terminalis in the formation of the zona intermedia of the adult. Thus this segment of the anorectal canal, which measures 5 to 12 mm. in length, is derived from the same anlage as the terminal urogenital tract. The crypts and columns of Morgagni develop in this area, and from the crypts tubular glandlike structures extend into the submucous and muscular layers of the rectum. These are called anal ducts or anal glands (fig. 3) and usually number less than six or eight. Gordon-Watson and Dodd⁹ pointed out that the glands grow outward into the

8. Pohlman, A. G.: Development of the Cloaca in the Human Embryo, *Am. J. Anat.* **12**:1, 1911.

9. Gordon-Watson, C., and Dodd, H.: Observations on Fistula in Ano in Relation to Perianal Intramuscular Glands, *Brit. J. Surg.* **22**:703, 1934.

loose tissue within the internal sphincter and into the limiting annulus of connective tissue which separates the internal sphincter above and the external sphincter below. They may spread to (1) the superficial surface of the levator ani muscle and into the ischiorectal fossa; (2)

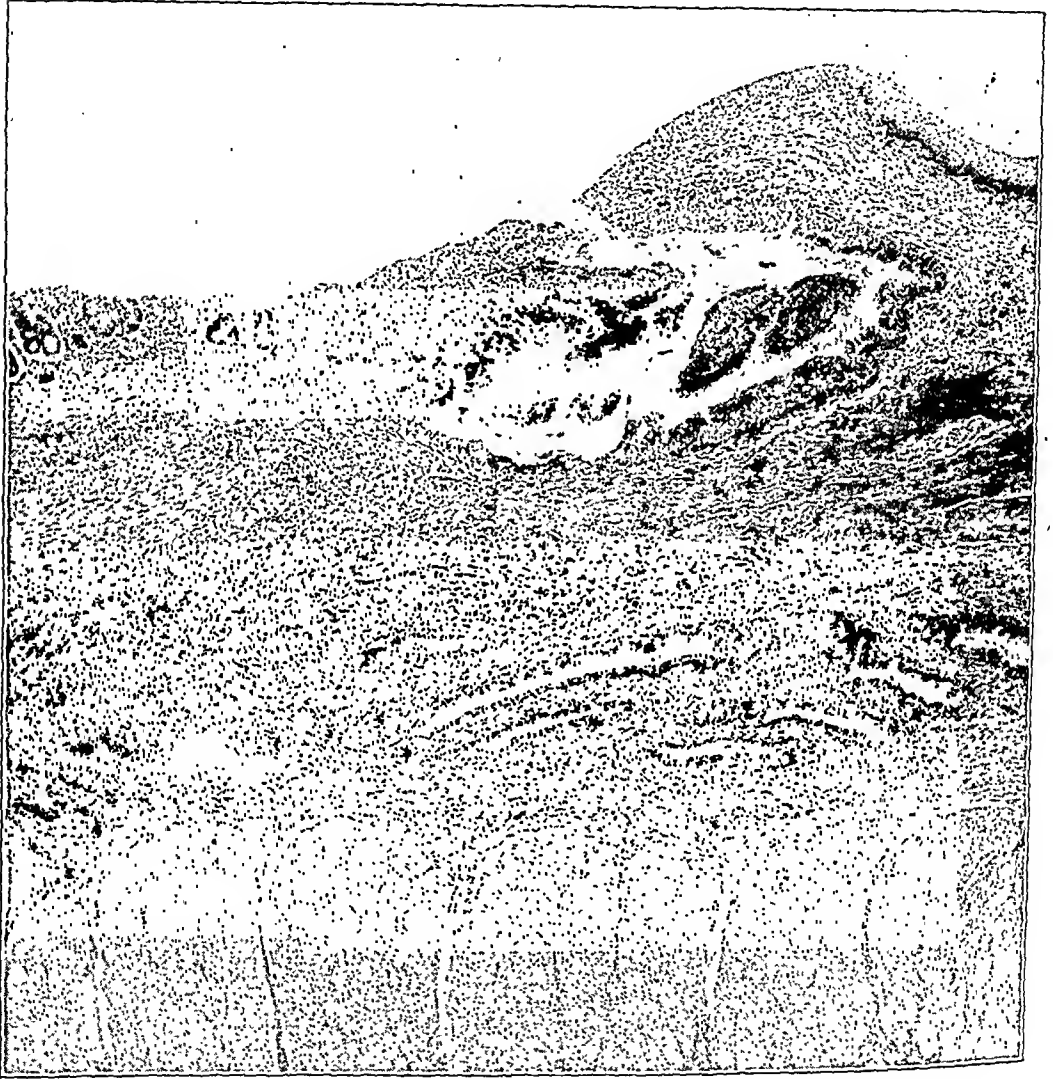


Fig. 3.—Section through the anorectal canal of an infant aged 1 month. Note the large crypt and beneath this the anal glands deep in the submucosa.

deep to the levator ani muscle and into the true pelvis, or (3) into the substance of the levator ani muscle. They are lined by several layers of polygonal cells in the main ducts and one to two layers of cuboidal cells in the branches. Mucin-secreting cells are usually present.

Misplacement of ectoderm¹⁰ during the formation of the caudal extremity, especially with improper closure of the dermal cleft or resorption of the cloacal membrane, may give rise to cysts of the perineum or the pelvic connective tissue or to raphes of the scrotum and penis.

It has been concluded by Vallois and Peyron¹¹ that a plexus of blood vessels derived from the embryonic vascular channels, similar to the caudal artery and its corresponding vein in lower animals, gives rise to the coccygeal glomus. It was formerly thought to consist of a single body measuring about 2.5 mm., lying in front of the apex of the coccyx. It is now known, however, that there may be several irregular sinusoid masses, which are very vascular. Masson¹² has described the neural and smooth muscle elements wrapped about an arteriovenous anastomosis similar to a subungual glomus.

DESCRIPTION OF CASES AND COMMENT

No tumors or cysts of the coccygeal medullary vestige or of notochordal vestiges are included in the present study.

Tail Gut Vestiges.—We prefer the term "tail gut" or "caudal gut" to "postanal gut" because it gives a more precise description of the origin and location of this structure. Peyron⁴ observed that the tail gut vestige in the caudate embryo consisted of a more or less elongated vesicle formed of intestinal epithelium containing mucous glands, lying below the anus and in front of the neurovascular structures (fig. 1 *D*). No distinct muscular or serous coats were present. He noted that considerable variation in the types of epithelium in any one specimen was possible and that this variation corresponded to the degree of metaplasia found in cysts arising from this vestige.

Peyron⁴ suggested that an anterior sacrococcygeal or retrorectal cyst containing an epithelial lining of the intestinal type (including cells which take the mucicarmine stain) and having no definite muscular or serous coat could be assumed to be of tail gut origin.

Middeldorpf¹³ in 1885 described a mucus-containing cystic postanal tumor the size of an egg, which was removed from a girl 1 year old. Histologically it was composed of areolar tissue and a fragment of intestine similar to normal intestine. Tubules, resembling Lieberkühn's

10. Ewing, J.: *Neoplastic Diseases*, ed. 3, Philadelphia, W. B. Saunders Company, 1928, p. 1036.

11. Vallois, H., and Peyron, A.: *Sur les premiers stades du développement du glomérule coccygien chez l'homme*, *Compt. rend. Acad. d. sc.* **170**:894, 1920.

12. Masson, P.: *Le glomus neuromyo-arterial des régions tactiles et ses tumeurs*, *Lyon chir.* **21**:257, 1924.

13. Middeldorpf, K.: *Zur Kenntnis der angeborenen Sacralgeschwülste*, *Virchows Arch. f. path. Anat.* **101**:37, 1885.

glands, and muscle layers were described. No serous coat was found. This case has been generally accepted as the first instance of a tumor of caudal gut origin to be reported in the literature.

Galletly¹⁴ in 1924 reported a carefully studied case which fulfils Peyron's criteria. A woman aged 43 presented a cyst between the coccyx and the gluteal region, which had been subjected unsuccessfully to local excision on several occasions. Laparotomy allowed complete removal. The wall of the cyst showed squamous epithelium with intracystic tufts composed of columnar cells of the intestinal type. Some granulation-like tissue and numerous foreign body giant cells were described.

Subsequently, several cases have been described. Among these are some which present features that make their inclusion in this group questionable and others that were incompletely described, making satisfactory interpretation impossible.

Thomason¹⁵ described 2 cases. From the description, the tumor in the first seems to have been of caudal gut origin. However, the author added: "The history of its having been removed at a previous operation suggests, of course, that our tumor whatever else it may be is a teratoma, perhaps a 'suppressed twin.'" The second case is almost devoid of any descriptive data. In it the condition was associated with several anomalies, such as an enlarged tail-like coccyx and nonfusion of the lamina of the first sacral vertebra.

In Robertson and Wride's¹⁶ case, the cyst contained bone and ganglion-like cells in addition to what was believed to be intestinal epithelium.

Ravin¹⁷ reported 1 case in which the condition occurred in an infant 2½ months old. His only comment was: "The cyst is lined with several layers of cells the innermost of which is columnar and ciliated."

Ballantyne¹⁸ has reported a carefully studied case which he regarded as an instance of carcinoma arising in a postanal gut vestige in a woman aged 38. Histologically the cyst showed an intestinal glandlike arrangement of lining composed of columnar epithelium. Goblet cells were present, and at one point frankly carcinomatous tissue was found.

14. Galletly, A.: Presacral Tumors of Congenital Origin, *Proc. Roy. Soc. Med. (Sect. Obst. & Gynec.)* **17**:105, 1924.

15. Thomason, T. H.: Cysts and Sinuses of the Sacrococcygeal Region, *Ann. Surg.* **99**:585, 1934.

16. Robertson, F. N., and Wride, G. E.: Case of Persistent Cyst of Postanal Gut Origin in an Adult, *Canad. M. A. J.* **31**:535, 1934.

17. Ravin, R. W.: Sacrococcygeal Cysts and Tumors, *Brit. J. Surg.* **23**:337, 1935.

18. Ballantyne, E. N.: Sacrococcygeal Tumors: Adenocarcinoma of Cystic Congenital Embryonic Remnant, *Arch. Path.* **14**:1 (July) 1932.

Records of 2 cases in which we believe the condition to have been of caudal gut origin are found in our files.

CASE 1.—A woman aged 26 complained of pain on defecation for three months and of pains vaguely located in the lower part of the abdomen for seven years. There had been rather severe constipation but no tenesmus. No pus, blood or mucus had been observed in the stool. The patient had undergone an appendectomy seven years before and a cyst had been removed from the left ovary two years before at another hospital.

Examination revealed a soft swelling to the left of the urethral orifice and an anal fistula 3 cm. in length opening into the posterior commissure at the mucocutaneous junction. The tract seemed to pass around to the left anterior rectal wall. No masses were noted. Incision and drainage of what was thought to be a submucous abscess were performed. The external sphincter was divided at the posterior commissure, and the sinus was packed with iodoform gauze.

The patient continued to have occasional rectal pain and constipation, but the wound healed satisfactorily. Seventeen months later, however, there was recurrence of acute anorectal pain, together with passage of a considerable quantity of pus and blood.

Examination showed an elevated bluish red area about 4 cm. from the anus on the posterior anorectal wall. Greenish yellow pus was seen exuding from an opening in this area. This was thought to represent a recurrent submucous abscess, and incision and drainage, together with curettage, were carried out. Unfortunately no pathologic studies were done at this time. Healing was unsatisfactory, and the patient was referred to Dr. Charles L. Janssen, who made the following note: "Just at the mucocutaneous junction a sharp-edged opening is felt. Above this an ovoid mass about 5 by 3 cm. is encountered. It is soft, not fluctuant and exquisitely tender. The size of the mass suggests the possibility of a cyst being associated with the abscess."

A third operation was performed one month later, at which time it was recognized that a rather large multilocular cyst or multiple cysts, some containing clear mucus and others caseous material, lay in the posterior rectal region. Complete excision was not attempted, but several portions were removed and the wound was packed with gauze. The postoperative course was complicated by a hemorrhage on the ninth day, together with cystitis and some psychotic manifestations. A more radical surgical procedure was planned, but subsequently the patient went to another hospital and was lost to the follow-up clinic.

Sections (fig. 4) of the specimen showed a multilocular cyst filled with material which took the mucicarmine stain. The epithelial lining elements showed metaplasia. Stratified squamous and stratified columnar cells were most numerous, and in some portions definite Lieberkühn crypts appeared. Frequent acini of clear columnar cells and many mucin-secreting cells were found. The arrangement definitely suggested intestinal mucous membrane. No cilia, intercellular bridges, keratohyaline granules or argentaffin cells were observed. Occasional scattered groups of smooth muscle bundles were present in the periphery, but no definite muscular or serous coats were found.

CASE 2 (Submitted by Dr. George H. Semken).—The patient was a woman aged 36. The tumor was found during the course of a gynecologic examination. It had given the patient no symptoms.

Digital examination revealed an ellipsoid mass at the left side of the rectum, just in front of the coccyx. It seemed well defined and encapsulated and was soft rather than fluctuant.

At operation it was found that the mass, which measured 2.2 by 1.8 cm., lay external to the fascia propria of the rectum and was partly incorporated in the coccygeal portion of the levator ani muscle. The tumor was easily removed, and convalescence was uneventful.

The specimen contained about 4 cc. of thick brownish material composed of degenerated epithelium and amorphous débris. Fibroareolar tissue covered the



Fig. 4 (case 1).—Section through a portion of a caudal gut cyst. Note the several types of epithelium present.

external surface of the cyst. The wall averaged 1 to 2 mm. in thickness, and the inner surface presented a smooth, almost velvety, appearance.

Sections (fig. 5) through the wall of the cyst showed it to be lined in part by three types of stratified epithelium: squamous, columnar and ciliated. The last two are mucin-secreting membranes. A definite tendency to glandular formation was seen in some areas. Elsewhere a granulation-like tissue containing large num-

bers of pigment-laden phagocytes formed the lining of the cyst. In the wall a few scattered smooth muscle fibers were seen. No keratinization, formation of intercellular bridges or other evidence that might suggest an ectodermal origin of this cyst was found.

CLOACAL VESTIGES

Anal Glands.—A large number of anal glands have been observed in conjunction with regional disease as well as incidental to the examina-

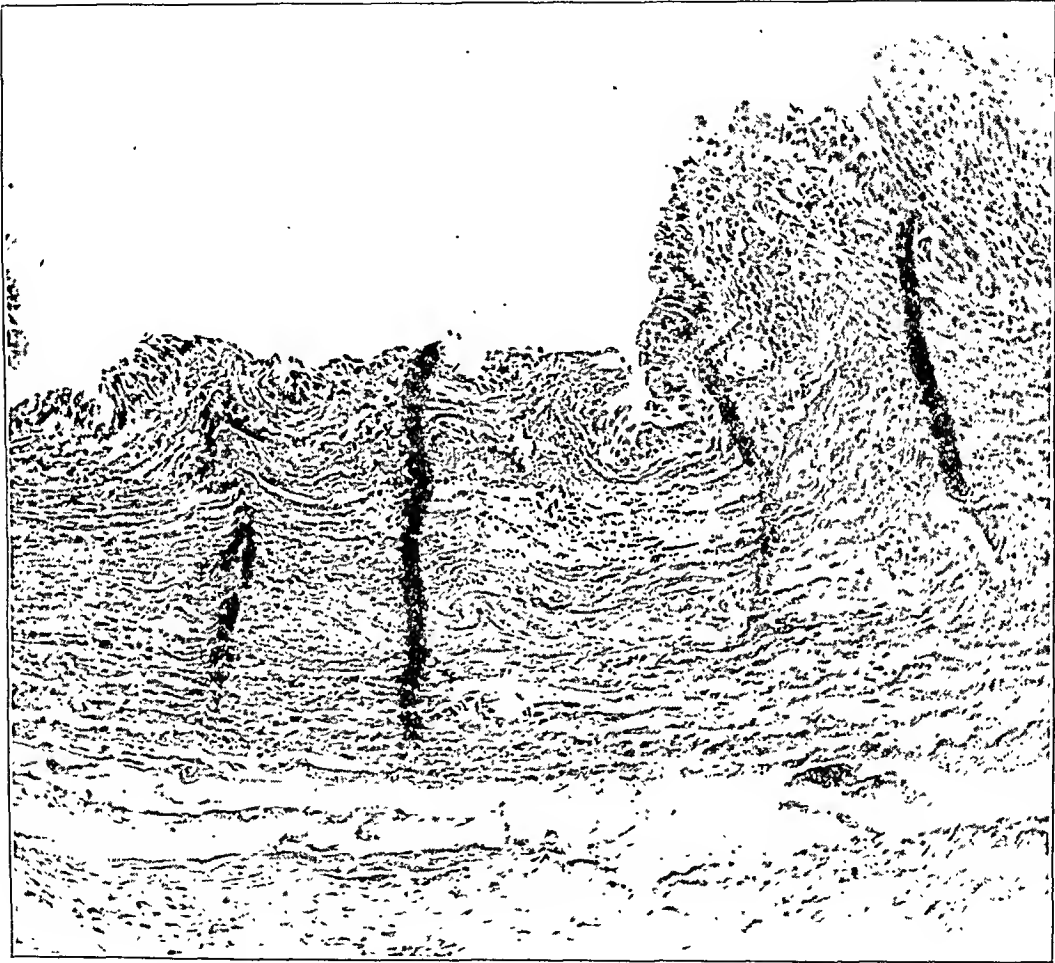


Fig. 5 (case 2).—Section through the wall of a caudal gut cyst.

tion of anorectal specimens. They seem to be vestiges of the primitive cloaca. The frequency with which they have been designated “super-numerary rectal glands,” “postanal gut fistulas,” “heterotopic rectal mucosa” and “epithelized fistulous tracts” in our series has prompted us to review these specimens in conjunction with the present study.

Herrmann and Defosses¹⁹ first suggested that fistula in ano might be caused by anal glands. Several brief studies appeared subsequently, and in 1929 Lockhart-Mummery²⁰ referred to them as a possible cause of fistula and pointed out that these structures had apparently been overlooked by anatomists and surgeons. Relatively few references to these obviously important structures appeared until, in 1930, Tucker and Hellwig^{21a, b} pointed out the fact that the crypts of Morgagni are not in themselves responsible for the frequency of anal infections. As a rule, these infections are due to the "anal ducts" which open into the crypts and provide a ready path for infecting organisms to enter the wall of the anal canal, resulting in cryptitis, periproctitis, fissures and fistulas. They noted that the anal ducts appear in the embryo at the same time as the prostate and periurethral glands and have a distinct histologic resemblance to these organs. In addition, they pointed out that the biologic characteristic of harboring the rather easily destroyed gonococcus is common to these related structures.

Two cases in which rather prominent anal glands were found are reported.

CASE 3.—A white man aged 36 complained of anal pain, pruritus and hemorrhoids of about four years' duration.

Examination revealed a chronic fissure in ano with a sentinel pile in the posterior commissure. About 1 cm. superior to the fissure a fistulous opening about 2.5 cm. in length was demonstrated. Internal hemorrhoids were also present.

At operation the tract was injected with methylene blue, and excision of the fissure and the fistula as well as of the hemorrhoids was performed.

The wound seemed to heal slowly, and several months later it was noted that a second fissure had appeared at the same site. Reoperation was performed, and ultimate healing occurred.

Sections (fig. 6) of the fistula revealed a large, tortuous compound glandular structure lined by stratified columnar epithelium, which arose from a depression in the mucocutaneous junction. Mucin-secreting cells were frequent, and inflammatory cells were numerous throughout the supporting tissue. It is probable that the first operation was incomplete and that some of the epithelium remained, causing delayed healing and secondary fissure formation.

CASE 4.—A Chinese man aged 50 was admitted to the hospital with the clinical diagnosis of carcinoma of the stomach with metastases to the liver. There were no anorectal complaints. On routine examination a soft nontender mass measuring 2 cm. in diameter was found in the submucosa of the anterior rectal wall, just above the internal sphincter. Proctoscopic examination revealed a punched-out ulcer 5 mm. in diameter in the mucosa covering the mass. The mass and the ulcer

19. Herrmann, G., and Defosses, L.: Sur la muqueuse de la région cloacale du rectum, *Compt. rend. Acad. d. sc.* **90**:1301, 1880.

20. Lockhart-Mummery, J. P.: Discussion on Fistula-in-Ano, *Proc. Roy. Soc. Med.* **22**:1331, 1929.

21. Tucker, C. C., and Hellwig, C. A.: (a) Anal Ducts, *Arch. Surg.* **31**:521 (Oct.) 1935; (b) Histopathology of Anal Crypts, *Surg., Gynec. & Obst.* **58**:145, 1934.

were excised, and the wound was closed. Convalescence was uneventful, but the patient succumbed to the intra-abdominal neoplasm about a year later.

Section of the specimen showed that the ulcer was situated slightly proximal to the mucocutaneous junction. Its base was covered with slough, and there was no granulation tissue or evidence of repair. At the mucocutaneous junction a large anal gland (fig. 7) wound about in a tortuous manner in the fibers of the



Fig. 6 (case 3).—Large anal glands associated with fistula and fissure in ano.

sphincter. It was lined with stratified columnar, mucus-producing epithelium, and in one or two places it blended with stratified squamous cells. There were no cilia. Several argentaffin cells were present in the mucosa of the anorectal canal but not in the glands. The sections did not indicate the cause of the ulcer; however, it is plausible to assume that the anal glands may have been associated with its production.

Vestiges of Cloacal Membrane.—The location of tail gut cysts is fairly well defined as retrorectal. Anterior rectal or perineal cysts may arise by persistence of remnants of the cloacal membrane or by heterotopia of the ectoderm of the dermal cleft. The presence of ciliated epithelium in cysts of vestigial origin is not particularly astonishing or



Fig. 7 (case 4).—Anal gland associated with rectal ulcer.

significant when it is recalled that ciliated epithelium is found lining many embryonal structures, such as neural, enteric, respiratory and genital canals (Ewing).

The cyst described in the following report we believe to have developed from the entoderm of the cloacal membrane.

CASE 5.—A white man aged 23 complained of a mass anterior to the anus, of many years' duration. There had been no noticeable changes in its size. During the week preceding his admission to the hospital the patient had observed a swelling in the sacrococcygeal region, associated with some pruritus.

Examination revealed a rounded pedunculated soft cystic mass about 2.5 cm. in diameter, attached to the anterior commissure of the anus. In addition, in the midline of the coccygeal region two very small openings were noted. There was some evidence of inflammation in this region. Digital and anoscopic examinations gave essentially negative results.

At operation the perineal mass was found to be adherent to the lower border of the external sphincter. It was easily removed. A sacrococcygeal cyst measuring 2.5 by 1.5 cm. was removed en masse. Recovery was uncomplicated.

The first specimen contained about 3 cc. of brownish yellow puslike material. The lining of the cyst was smooth and glistening. Microscopically (fig. 8) the lining showed a rather even stratified columnar ciliated epithelium with some evidence of the secretion of mucin. There was no definite suggestion of gland formation, and no epithelial metaplasia. In the fibrous tissue of the wall some smooth muscle was found.

The second specimen contained some amorphous material and a few hairs. Its lining was composed entirely of granulation tissue in which many foreign body giant cells were noted.

The perineal cyst would seem to be of cloacal rather than intestinal origin. The fact that no glands were present, as well as the anterior location of the cyst, would exclude the caudal gut vestige as a possible source of origin. Its association with a sacrococcygeal sinus is unusual but not remarkable. There is no evidence that the lesions were in any way related. The absence of epithelium in the sinus was probably due to the destructive influence of the inflammatory process which prompted the patient to seek medical treatment.

CASE 6.—A white woman aged 35 stated that she had first noticed a growth near the anus a year before. It had given slight pain and had bled on one occasion. Pruritus had been severe.

Examination revealed two tabs of skin attached to the posterior commissure of the anus. The larger of these tabs measured 1 cm. in diameter.

At operation a tract about 4 cm. in length was found arising from one tab and extending outside the external sphincter. The tract was sectioned, and several drops of pus escaped from it. Methylene blue was injected, but no internal opening could be discovered.

Convalescence was uneventful, and the sinus healed.

Sections (fig. 9 and 10) through the larger tab showed that it contained two cysts, which differed histologically. One cyst was lined with stratified cuboidal and columnar epithelium. Many of the surface cells contained droplets of mucin. At intervals ciliated cells were found, isolated or in groups. Occasional cells in the basal layer contained granules which blackened with silver and had the appearance and characteristics of argentaffin cells. There was a tendency to squamous cell metaplasia in some areas, but no keratinization was found. Surrounding this cyst were great numbers of phagocytic cells the cytoplasm of which was distended by large numbers of coarse brown granules. From their staining reaction to scarlet red it is believed that they were lipoids.

In another portion of the cutaneous tab and apparently not communicating with the cyst just described was a second cyst (fig. 10). It was in part lined with stratified squamous epithelium, the flattened surface cells of which were hydropic and vacuolated and contained no keratohyaline granules. The basal layer of cells contained no melanin. In another portion of the cyst, stratified columnar cells were present. In a third part, no epithelium was found; instead, a loose, relatively

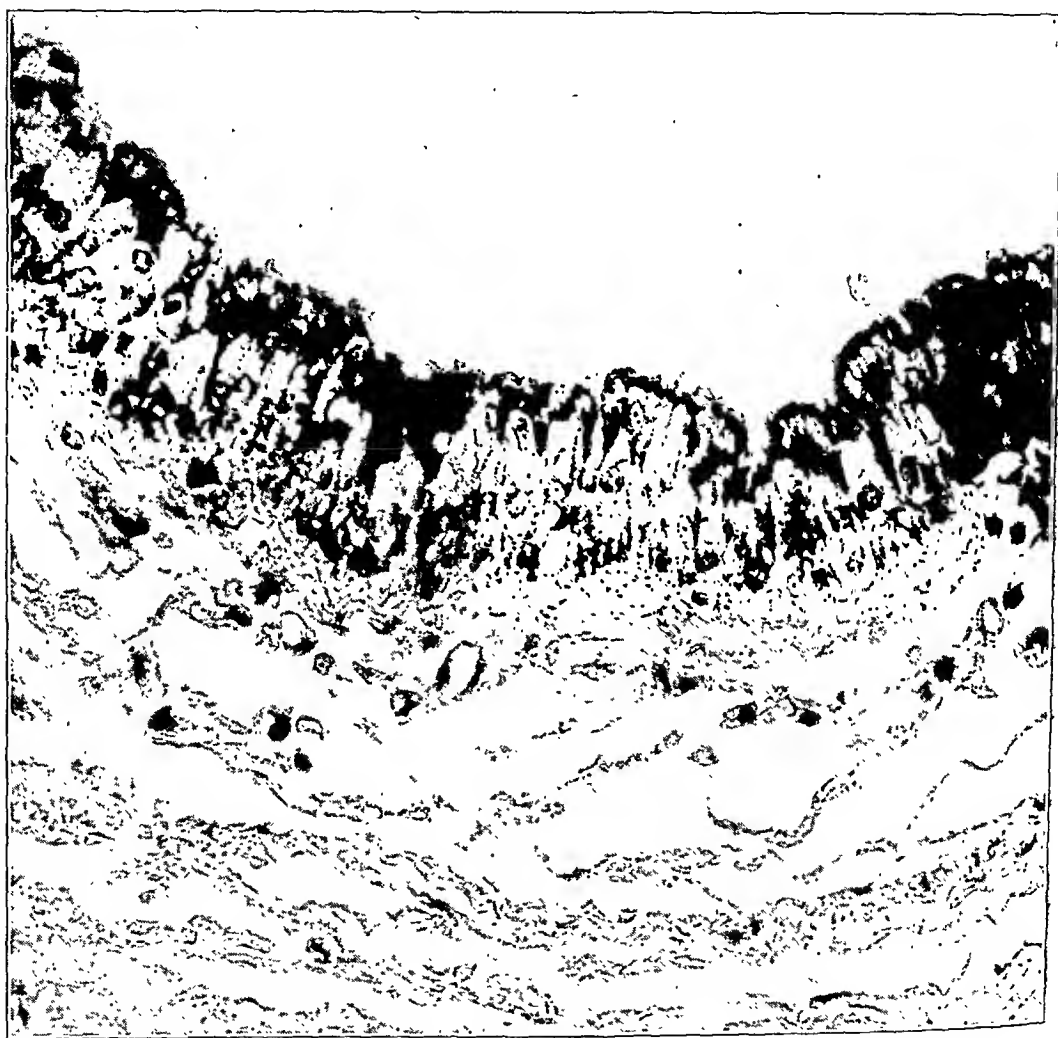


Fig. 8 (case 5).—Section through the wall of a cyst of the cloacal membrane. Note the cilia present.

avascular network of fibrous tissue containing large numbers of foam cells formed the wall of the cyst.

The definite histologic differences between these cysts would seem to indicate that they arose from different anlagen. The presence of silver-positive cells which appeared to be argentaffin cells within one of the

cysts is the only observation which suggests intestinal origin. The distinct histologic resemblance of this cyst to that in the previous case leads us to believe that it was probably a vestige of the cloacal membrane. The second cyst almost certainly arose from heterotopia of the ectoderm of the dermal cleft.



Fig. 9 (case 6).—High power photomicrograph of a section through a cyst of the cloacal membrane.

SUMMARY

The development of the caudal portion of the body is attended by numerous complex processes involving the medullary tube, the primitive intestinal tract, the notochord and the cloaca. Disturbances in development may lead to persistence of certain embryonal vestiges, which are

sometimes important factors in the production of cysts, tumors and fistulas of this region. From the number of cases reported in the literature one would judge that the persistence of vestiges is rare; however, they are probably more common than this would indicate. Vestiges of the cloaca are normally found in the anorectal canal, form-

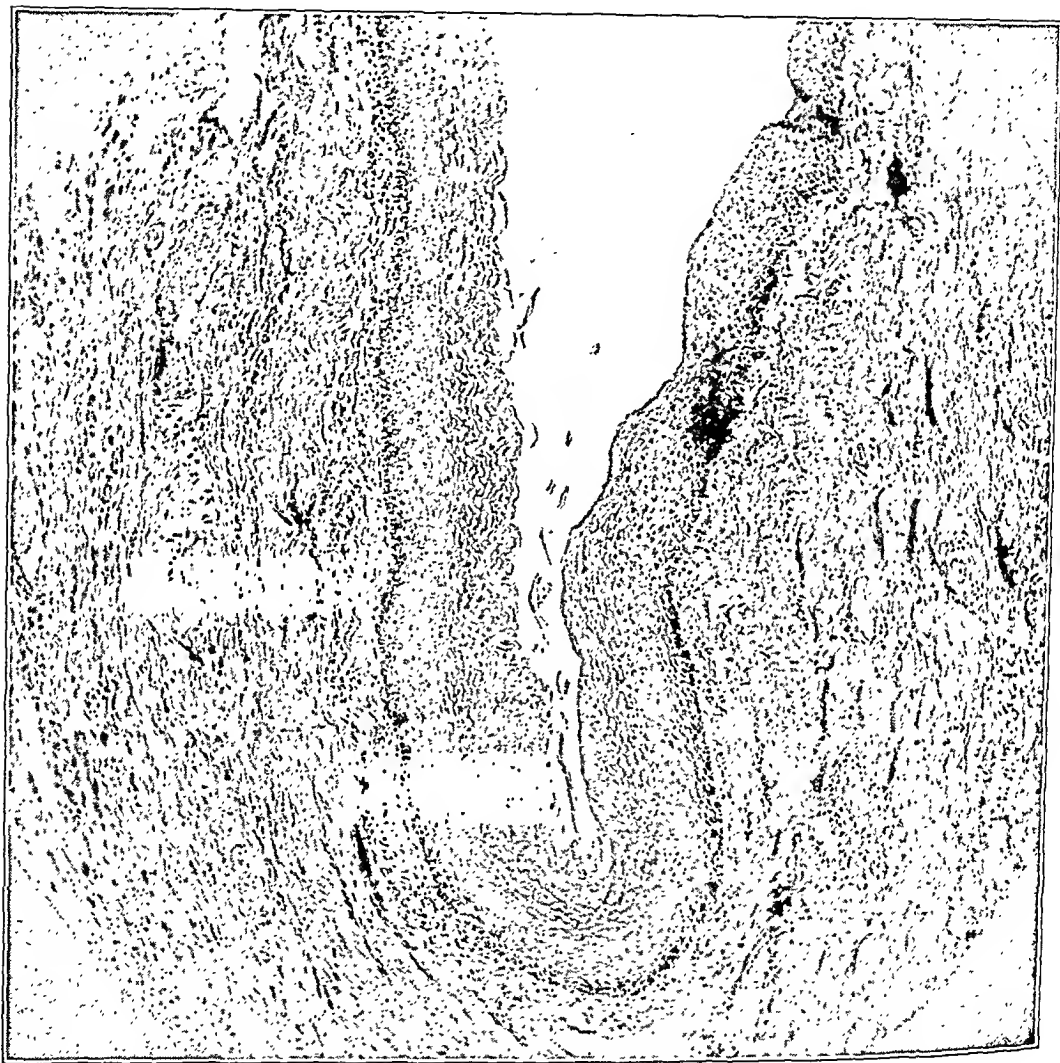


Fig. 10 (case 6).—Section through a cyst of ectodermal origin found adjacent to the cyst shown in figure 9.

ing the anal glands, which are extremely important in the causation of lesions of this area.

The histologic and topographic features of caudal gut cysts, as well as of cloacal cysts, are discussed. Two representative cases of each group are reported, and illustrative cases in which there were large anal glands are cited.

CONCLUSIONS

1. The presence of cysts of the perianal region can be explained on an embryologic basis, and the cysts may be classified according to their source.
2. Cysts of a single germ layer which are of embryonal origin may be derived from the caudal gut, the cloaca or the ectoderm of the dermal cleft.
3. Vestigial structures, such as the anal glands, are frequent sites of anorectal lesions, such as fistula, fissure and perirectal abscess.

MOTION OF THE LUNG AFTER SURGICALLY INDUCED PARALYSIS OF THE PHRENIC NERVE

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Differences of opinion are still encountered as to the mechanical effect of induced paralysis of the hemidiaphragm on the volume and function of the corresponding lung. Yates¹ expressed the opinion that the motion of the parietes of the chest can be limited by blocking the nerve trunks which transmit motor impulses to the diaphragm. He stated that surgical paralysis and consequent atony of the diaphragm induce a reduction in the movements of the thoracic parietes of the chest or, even if there are adhesions, a reduction in the volume of the lung, and the pulmonary excursions are limited to those immediately above and below the mean inflation. Lilienthal² said that clinical results and roentgenologic appearances led him to the conclusion that the elevation of the diaphragm after having crushed the phrenic nerve may effect a reduction in capacity the equivalent of from 200 to 500 cc. and also a decrease in the respiratory excursions. Bettman³ recommended phrenicoexeresis for obtaining collapse and rest of the diseased lung. He estimated that the diminution of thoracic volume by the rise of the paralyzed diaphragm in an adult varies somewhere between 400 and 600 cc. Alexander⁴ contended that mere relaxation of the lung and reduction of its volume necessarily cause a certain amount of pulmonary rest; elimination of the pumping function of the diaphragm, he said, is the most important single factor in resting the lung. He quoted Berard, who estimated that the volume of the lung is reduced from one fourth to one third by phrenicotomy, and Ziegler, whose estimate is one fourth.

Wilson⁵ tabulated the data of other investigators concerning the influence of the diaphragm and the ribs on the normal respiratory

From Muirdale Sanatorium.

1. Yates, J. L.: Operations as Aids in the Treatment of Pleuropulmonary Tuberculosis, *Ann. Surg.* **86**:200, 1927.

2. Lilienthal, H.: Mechanical Principles of the Operative Treatment of Pulmonary Tuberculosis, *Ann. Surg.* **86**:182, 1927.

3. Bettman, R. B.: Phrenectomy, *Illinois M. J.* **52**:374, 1927.

4. Alexander, J.: The Surgery of Pulmonary Tuberculosis, Philadelphia, Lea & Febiger, 1925.

5. Wilson, H., cited by Graham, E. A.; Singer, J. J., and Ballon, H. C.: Surgical Diseases of the Lung, Philadelphia, Lea & Febiger, 1935, p. 455.

volume. These data reveal that the diaphragm contributes from 37 to 47 per cent of the volume of respired air on quiet respiration. Eloesser and Brown⁶ expressed the opinion that pulmonary rest is not very great after phrenicotomy. Straub⁷ found that the loss of pulmonary volume which accompanies paralytic elevation of the dome of the diaphragm amounts to from 20 to 30 per cent. He stated that although a phrenic operation results in a certain amount of relaxation and immobilization of the corresponding lung, it carries with it the disadvantage of not absolutely eliminating the motion of the lung on account of the compensatory thoracic motion during respiration. It was shown by Schnippenkotter⁸ and by Head⁹ that the paralysis of the hemidiaphragm is compensated for chiefly by increased action of the homolateral ribs. Lambert¹⁰ emphasized that the extent of the rise of the diaphragm should not be taken as the sole criterion on which to judge the efficacy of surgical operation on the phrenic nerve in any given case. The conception he expressed was that elimination of the phrenic pathway interrupts an important link in the mechanism coordinating the various factors of the respiratory function and thus leads the intercostal and abdominal muscles to act less vigorously. He stated the belief that this consequence, together with the loss of the contractile power of the diaphragm, results in a diminution of pulmonary expansion and contraction during respiration and effects a certain degree of rest in the pulmonary tissue.

Sisti and Soricelli¹¹ made kymographic studies of the chest before and after crushing of the phrenic nerve and were able to demonstrate that the excursions of the ribs increased after operation. The experimental studies of Strauss¹² led him to the conclusion that induced paralysis of the phrenic nerve does not immobilize the lung. A similar opinion was expressed recently by van Joost,¹³ who said that the lack

6. Eloesser, L., and Brown, P. K.: Surgical Intervention in Pulmonary Tuberculosis: Pathological Conditions in the Lung and the Various Forms of Operations Applicable to Them, *Am. Rev. Tuberc.* **8**:519, 1924.

7. Straub, G. F.: *Surgery of the Chest*, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

8. Schnippenkotter, W.: Surgical Paralysis of the Diaphragm, *Beitr. z. Klin. d. Tuberk.* **65**:56, 1926.

9. Head, J. R.: The Redistribution of Respiration Following Paralysis of the Hemidiaphragm, *Surg., Gynec. & Obst.* **50**:929, 1930.

10. Lambert, A. V. S.: Results of Operation Which Interrupts Nerve Impulses Along the Phrenic Nerve Pathway, *J. Thoracic Surg.* **4**:49, 1934.

11. Sisti, M. A., and Soricelli, F.: Roentgen-Kymographic Studies Following Phrenic Nerve Block, *Arch. di radiol.* **12**:108, 1936.

12. Strauss, L. H.: Effect of the Exeresis of the Phrenic Nerve, *Beitr. z. Klin. d. Tuberk.* **88**:374, 1937.

13. van Joost, C. R. N. F.: Notes on Phrenic Nerve Paralysis in the Treatment of Pulmonary Tuberculosis, abstracted, *Zentralbl. f. d. ges. Tuberk.-Forsch.* **46**:517, 1937.

of major immobilization of the lung following block of the phrenic nerve is due to the immediate compensatory ventilation induced by the increased motion of the ribs. Furthermore, Matson and Matson¹⁴ stated that the beneficial effect of hemidiaphragmatic paralysis is due to the degree of collapse obtained in the diseased lung by the rise of the corresponding side of the diaphragm, rather than to any rest provided.

NEW METHOD OF STUDY

The object of the study reported in this paper was to ascertain the extent of motion of the treated lung by a new method for the determination of the respiratory expansion of the chest, devised by Hurtado and Fray.¹⁵ They found that the degree of thoracic expansion can be estimated from the relation between the roentgenologic pulmonary fields at maximum expiration and inspiration. The roentgenograms used in my work were taken at the end of the two respiratory phases in the upright position on two films from a distance of 6 feet (180 cm.). The area of the fields was measured by means of a planimeter, the tracer of which was moved along the inner aspect of the ribs on the following course: from the left axilla, through the left half of the diaphragm, the right half of the diaphragm, the right lateral border of the lung and the right apex, and across the spine to the starting point at the left apex. A line was drawn corresponding to the position of the trachea and the mediastinal borders of the two lungs. Thus it was possible to measure the areas of the diseased and the "good" lung separately.

The figures on the differential wheel of the planimeter used indicate area in square centimeters. The roentgenologic respiratory ratio; R. R. R., was calculated according to the following formula: (roentgenologic area at maximum expiration/roentgenologic area at maximum inspiration) \times 100. This ratio is inversely proportionate to the extent of the respiratory excursions: The higher the ratio, the smaller the motion, and vice versa.

Hurtado and Fray¹⁵ stated that if the ratio thus calculated is higher than 72, a definite reduction in chest expansion may be suspected. My calculations showed that the ratio of the diseased lung before operation varied from 60 to 98. In 30 cases analyzed 2 values were between 60 and 69, 8 between 70 and 79, 14 between 80 and 89 and 6 90 or more. The roentgenograms were taken one month after operation in 25 cases, after a four-day interval in 2 (1 case of exeresis and 1 of

14. Matson, R. C., and Matson, R. W.: Phrenic Neurectomy, in Goldberg, B.: *Clinical Tuberculosis*, Philadelphia, F. A. Davis Company, 1935.

15. Hurtado, A., and Fray, W. W.: Studies of Total Pulmonary Capacity and Its Subdivisions, *J. Clin. Investigation* 12:807, 1933.

phrenemphraxis), after a sixteen-day interval in 1 (phrenemphraxis), after a two and one-half month interval in 1 (phrenemphraxis), and after an eight-month interval in 1 (exeresis). Dr. F. Raine, visiting surgeon to the Muirdale sanatorium, performed all operations. I estimated the postoperative motion of the lung by comparing the ratios of both lungs after operation with the ratios of both lungs before operation. It must be remembered, however, that without due correction such a comparison may give a false impression. The force of the inspiratory and expiratory efforts may differ before and after operation. The true value of the motion of the diseased lung is determinable only if one corrects the areas according to the extent of motion on the "good" side.

An example may illustrate this point. Assume that before operation the expiratory area was 153 sq. cm. and the inspiratory area 191 sq. cm. on the "good" side; its R. R. R.: $\frac{153}{191} \times 100 = 80$. The diseased side had at the same time an expiratory area of 167 sq. cm. and an inspiratory area of 200 sq. cm.; its R. R. R.: $\frac{167}{200} \times 100 = 83$. The respiratory motion of the diseased lung is 3 (83—80) points less than that of the "good" lung. After operation, the expiratory area of the "good" lung is 142 sq. cm. and the inspiratory area is 184 sq. cm.; its postoperative R. R. R.: $\frac{142}{184} \times 100 = 77$. The motion increased by 3 (80—77) points when compared with the preoperative function. After operation, the diseased lung had an expiratory area of 153 sq. cm. and an inspiratory area of 168 sq. cm.; its postoperative R. R. R.: $\frac{153}{168} \times 100 = 91$. The motion decreased by 8 (91—83) points when compared with the preoperative function. The side not operated on shows a 3 point increase in motion while the side operated on has an 8 point decrease. In other words, as the result of operation, the side operated on has an 8 point decrease in motion instead of the 3 point increase of the side not operated on, that is, a *gain in rest* of 11 (8+3) points. The figure calculated according to this formula is designated as the relative index of motion of the lung operated on.

RESULTS OBTAINED BY NEW METHOD

My results show that the motion of the lung after induced paralysis of the corresponding phrenic nerve was reduced in 18 cases (60 per cent), remained unchanged in 5 (16.7 per cent) and increased in 7 (23.3 per cent). It is evident that 12 patients (40 per cent) did not derive from the operation the rest anticipated. All patients with an R. R. R. of 0 or 1 were considered as having the motion unchanged. The extent of the increased motion varied from 4 to 14 points. Of the 7 patients with increased motion, 2 had undergone exeresis and 5

temporary nerve block (phrenemphraxis). In the 18 instances in which postoperative motion of the lung was reduced, the degree of reduction was predominantly slight or moderate. It was less than 5 points in 5 cases (16.7 per cent of all the cases analyzed), between 5 and 9 points in 8 (26.6 per cent), between 10 and 14 in 4 (13.3 per cent) and between 15 and 19 in 1 (3.3 per cent). Only 4 of the 30 patients had undergone exeresis; of these increased motion was noted after operation in 2 (50 per cent). Of the 26 cases in which there was temporary paralysis, the pulmonary motion became decreased in 16 (61.5 per cent), remained unchanged in 5 (19.2 per cent) and increased in 5 (19.2 per cent). Of the 8 right-sided temporary blocks, the postoperative motion of the lung decreased in 4 (50 per cent), remained unchanged in 1 (12.5 per cent) and increased in 3 (37.5 per cent); of the 19 left-sided temporary blocks, the motion decreased in 12 (66.6 per cent), remained unchanged in 4 (22.2 per cent) and increased in 2 (11.1 per cent).

The actual rise of the diaphragm after operation on inspiration was 4 cm. or more in 4 cases, 3 to 3.9 cm. in 10, 2 to 2.9 cm. in 4, 1 to 1.9 cm. in 7, less than 1 cm. in 2 and absent in 3. On expiration the actual rise was 4 cm. or more in 2 cases, 3 to 3.9 cm. in 1, 2 to 2.9 cm. in 7, 1 to 1.9 cm. in 11, less than 1 cm. in 8 and absent in 1. Excursions of 0.2 cm. were classified as "motion absent." The relative rise of the diaphragm (corrected according to the motion of the diaphragm on the "good" side) was 4 cm. or more on inspiration in 7 cases, 3 to 3.9 cm. in 6, 2 to 2.9 cm. in 9, 1 to 1.9 cm. in 4, less than 1 cm. in 1 and absent in 3. The relative rise on expiration was 4 cm. or more in 1 case, 3 to 3.9 cm. in 5, 2 to 2.9 cm. in 6, 1 to 1.9 cm. in 8, less than 1 cm. in 7 and absent in 3.

The actual postoperative motion of the corresponding dome of the diaphragm decreased in 21 cases (70 per cent), remained unchanged in 4 (12.6 per cent) and increased in 5 (16.7 per cent). The increase amounted to from 27 to 266 per cent of the extent of the preoperative motion. The increased diaphragmatic motion is explainable by one or more of the following factors: (1) tug of the opposite diaphragm, (2) release of adhesions and (3) artificial pneumothorax on the side operated on. Two of the patients had simultaneous contralateral artificial pneumothorax, another bilateral artificial pneumothorax and two others homolateral artificial pneumothorax.

A comparison was made between the preoperative motion of the diaphragm and the postoperative motion of the affected lung. We found that, with the exception of 1 case in the group with motion of 2 to 2.9 cm. and 1 case in the group, with motion of 3 to 5 cm., all cases with increased or unchanged pulmonary motion were ones in which the preoperative diaphragmatic motion was less than 2 cm. In

3 instances actual diaphragmatic motion was absent postoperatively; still the relative motion of the lung was reduced by from 3 to 9 points.

In the group in which the postoperative diaphragmatic motion was less than 1 cm., the reduction of the pulmonary motion varied from 0 to 12 points, and it was increased in 2 instances 6 and 14 points respectively. In the group with postoperative diaphragmatic motion of 1 to 1.9 cm., the pulmonary motion was reduced by from 1 to 14 points. In the group with diaphragmatic excursions of 3 to 5 cm., the reduction of the motion of the lung varied between 0 and 19; a 4 point increase occurred in 1 instance and a 7 point increase in another.

Considering the relation between the R. R. R. of the treated lung before and after operation, we found, except in 1 instance, no postoperative increased motion in cases in which the preoperative R. R. R. was less than 80. The reduction of motion in the group with an R. R. R. of 60 to 69 varied from 3 to 8, and in the group with an R. R. R. of 70 to 79 from 1 to 19; increased motion was noted in 1 case. Of the 14 cases with a preoperative R. R. R. of 80 to 89 the postoperative pulmonary motion increased in 5; in the group of 6 cases with a preoperative R. R. R. of 90 or more motion increased in only 1.

The relation between the type pulmonary or pleural disease and the postoperative motion of the lung was also studied. Of the 2 patients who were operated on because of tuberculous plastic pleurisy, 1 showed decreased pulmonary motion after operation and the other showed increased motion. Of the 6 cases of minimal pulmonary involvement, the motion decreased in 4, increased in 1 and was unchanged in 1. Of the 16 cases of moderately advanced involvement, in 10 the motion decreased, in 3 it increased and in 3 it remained unchanged. Of the 6 cases of far advanced involvement, decreased motion was observed in 3, increased motion in 2 and unchanged motion in 1. The influence of basal pleural adhesions that were demonstrable on the roentgenogram is reflected by the following data: Of the 11 cases belonging to this group, increased postoperative motion was noted in 4 (36.3 per cent) and unchanged motion in 2 (18.1 per cent). The degree of increased motion ranged from 5 to 14 points. Reduced motion was present in 5 cases (45.4 per cent).

SUMMARY AND CONCLUSION

A roentgenologic study of the change in the motion of the lung after surgical operation on the phrenic nerve is presented.

The analysis was made according to the new method of Hurtado and Fray, by determining the roentgenologic respiratory ratio (R. R. R.), that is, by calculating the relation between the roentgenologic area of the lung on maximum expiration and that on maximum inspiration.

The relative (or comparative) roentgenologic index of motion is shown to be a closer reflection of the true dynamics of a lung that has been operated on than those figures which express the actual difference in extent of motion without regard to increase or decrease in respiratory excursions of the lung not subjected to operation.

Although it is realized that the data presented in this work bear the limitations of a study based on a small number of cases, they throw some light on the question of pulmonary rest after operation on the phrenic nerve. I found that the motion of the lung after induced paralysis of the corresponding phrenic nerve decreased in 18 cases (60 per cent), remained unchanged in 5 (16.7 per cent) and increased in 7 (23.3 per cent). In other words, the anticipated postoperative pulmonary rest was not accomplished in 40 per cent of the cases.

EXPERIMENTAL PYLORIC AND JEJUNAL OBSTRUCTIONS

ABSORPTION OF SODIUM CHLORIDE FROM THE STOMACH AND THE UPPER PART OF THE SMALL INTESTINE

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Previous experimental work¹ has suggested that absorption of water from the stomach and the upper part of the small intestine in the presence of organic obstruction may be of some therapeutic importance. Dogs with obstruction of the upper part of the jejunum, 15 cm. below the ligament of Treitz, lived more than twice as long as animals receiving nothing by mouth and lost less weight when permitted to drink water. This indicates that water was absorbed from the upper part of the intestinal tract, in spite of obstruction and continued vomiting.

A series of experiments has been done to determine the effect on the length of life of animals with jejunal obstructions of drinking a solution of sodium chloride, a solution of 10 per cent alcohol and a combination of alcohol and solution of sodium chloride. In a second series the pylorus was obstructed and a comparison made of the chemical changes in the blood of animals receiving solution of sodium chloride and water.

TECHNIC OF EXPERIMENTS

Series 1.—Obstruction of the jejunum 25 cm. below the ligament of Treitz was produced by sectioning the intestine and turning the ends in with purse string sutures. Immediately after they recovered from the anesthesia all animals were given as much solution as they would drink. Vomiting was frequent and continued throughout the experiments. The animals in this series were divided into four groups of 6 each. The first group was given tap water only, the second group 0.6 per cent solution of sodium chloride, the third group 10 per cent solution of alcohol and the fourth group a combination of 10 per cent alcohol and 0.6 per cent solution of sodium chloride.

Series 2.—Obstruction was produced at the pylorus by sectioning the pyloric ring and closing the gastric and the duodenal end with a double row of silk

From the Department of Surgery, University of Kansas School of Medicine.

1. Carlson, H. E., and Orr, T. G.: Experimental Obstruction of the Jejunum: Effect of Administration of Water on Length of Life and Changes in Chemical Composition of Blood, *Arch. Surg.* **28**:292 (Feb.) 1934.

TABLE 1 (Series 1).—*Obstruction of the Jejunum 25 cm. Below the Ligament of Treitz*

Blood						Blood						
Dog No.	Day After Operation	Mg. per 100 Ce.			CO ₂ Combining Power, Vol. per Cent	Dog No.	Day After Operation	Mg. per 100 Ce.			CO ₂ Combining Power, Vol. per Cent	
		Total Non-protein Nitrogen	Chlorides (Whole Blood)	Creatinine				Total Non-protein Nitrogen	Chlorides (Whole Blood)	Creatinine		
Group 1 (water given by mouth as desired)												
1	0	36.4	530	1.0	46.6	4	6	27.0	405	0.8	69.2	
	2	30.9	450	1.0	57.9		8	40.6	340	0.9	74.9	
	4	43.6	400	1.0	69.2							
2	6	44.8	385	0.9	69.2	5	0	37.0	485	1.0	42.8	
	0	25.3	500	1.1	40.9		1	33.8	420	1.0	57.9	
	2	29.7	440	1.1	55.1		4	35.1	415	1.0	60.7	
	4	31.2	380	1.0	60.7		6	36.1	360	0.9	74.9	
	7	63.1	275	1.0	74.9		8	49.2	305	0.9	83.4	
	9	238.0	180	1.0	69.2		11	53.6	300	1.2	105.1	
3	0	27.0	495	0.9	65.5	13	48.2	265	1.1	100.8		
	2	27.3	455	1.0	58.9	15	46.8	300	1.0	106.4		
	4	28.9	410	1.0	68.3	18	61.8	225	1.0	102.6		
	6	43.6	310	0.8	84.3	20	75.8	200	1.1	100.8		
	8	85.6	220	0.9	99.4	6	0	28.3	485	1.0	54.1	
	10	59.5	260	0.9	95.0		2	31.9	395	1.0	55.1	
4	0	40.8	510	0.8	59.8		4	28.9	410	0.9	65.5	
	2	24.9	430	0.8	61.7		6	28.5	370	1.0	72.1	
	4	33.0	390	0.8	67.3		8	37.5	350	1.0	78.7	
							11	30.0	295	0.9	83.4	
					13	24.6	260	1.0	78.0			
					15	63.1	250	1.0	77.7			
Group 2 (0.6 per cent sodium chloride given, as much as animal would drink)												
1	0	25.7	510	1.1	45.7	4	0	20.8	450	0.8	55.1	
	2	28.5	410	1.1	70.2		2	27.0	440	0.9	61.7	
	4	34.3	380	1.1	80.6		4	24.5	430	0.9	69.2	
	6	34.3	410	1.1	76.8		6	18.2	465	0.8	69.2	
	8	43.2	350	1.1	84.3		8	19.6	370	1.0	59.8	
	10	32.8	260	1.2	86.2		10	16.2	450	0.9	56.0	
	12	53.6	305	1.0	90.0		13	16.1	500	1.0	53.2	
	14	43.6	330	0.9	92.2		15	42.2	485	1.7	49.4	
	16	35.5	320	0.9	98.8		5	0	26.9	530	1.0	47.5
	18	33.0	320	1.0	97.0			1	25.6	455	0.0	60.7
	20	27.3	385	0.9	81.8			4	32.8	450	0.9	62.6
2	0	35.5	500	1.1	44.7	6		29.0	440	0.9	72.1	
	2	33.3	425	1.3	62.6	8		35.9	410	0.8	72.1	
	4	34.5	440	1.1	64.5	11		41.9	375	1.0	95.6	
	6	30.3	480	1.1	62.6	13	46.8	325	1.0	95.0		
	8	32.3	495	1.2	60.7	15	34.7	370	1.1	93.2		
	10	33.2	450	0.9	68.3	18	35.9	360	1.0	85.6		
	12	42.2	425	1.2	66.4	20	38.0	320	1.0	97.0		
	14	136.3	395	1.4	89.0	22	30.0	365	1.4	80.8		
16	73.9	405	1.1	87.6	25	28.1	375	1.7	72.4			
18	145.7	415	1.2	85.6	27	26.8	380	1.0	79.8			
3	0	30.7	460	1.2	55.1	29	30.5	385	1.0	89.4		
	2	37.0	430	1.0	63.6	32	22.9	365	0.9	74.4		
	4	27.8	490	1.0	63.6	34	33.7	350	0.9	88.9		
	6	31.2	475	0.9	62.6	36	17.4	300	1.0	80.0		
	8	29.4	450	1.0	70.2	6	0	42.1	470	1.0	53.2	
	10	40.0	425	0.9	76.2		2	35.5	425	0.9	62.6	
	13	37.0	445	1.1	70.6		4	33.5	510	1.1	57.0	
	15	36.8	440	0.9	76.8		6	28.2	460	1.0	59.8	
	17	30.5	445	0.9	77.7		8	31.2	400	1.0	66.4	
	19	33.9	425	1.0	80.6		11	35.5	400	1.0	81.8	
	21	32.8	460	1.0	74.9		13	31.4	430	1.0	68.6	
	24	34.5	440	1.1	73.8		15	28.2	420	2.0	73.0	
	26	35.3	430	1.1	76.8		18	32.5	430	1.0	81.5	
	28	30.0	450	1.0	72.1		20	27.3	375	1.0	76.2	
	31	32.8	475	0.9	76.8		22	36.8	425	1.0	76.2	
	33	28.1	420	0.9	73.0		25	42.2	446	1.0	63.6	
	35	34.5	420	0.9	81.5		27	55.9	470	0.9	63.6	
	37	37.2	430	0.9	84.3							
	41	41.0	440	0.9	89.0							

TABLE 1 (Series 1).—Obstruction of the Jejunum 25 cm. Below the Ligament of Treitz—(Continued)

Blood						Blood						
Dog No.	Day After Operation	Mg. per 100 Cc.			CO ₂ Combining Power, Vol. per Cent	Dog No.	Day After Operation	Mg. per 100 Cc.			CO ₂ Combining Power, Vol. per Cent	
		Total Non-protein Nitrogen	Chlorides (Whole Blood)	Creatinine				Total Non-protein Nitrogen	Chlorides (Whole Blood)	Creatinine		
Group 3 (10 per cent alcohol given, as much as animal would drink)												
1	0	58.3	500	1.2	47.5	3	14	88.2	300	1.0	87.2	
	2	24.3	430	1.0	57.9		17	95.0	255	1.0	82.4	
	4	32.6	380	1.1	68.3		19	251.2	225	2.3	63.0	
	6	52.6	320	1.1	74.0		4	0	30.5	525	1.0	47.5
	8	81.2	300	1.0	82.5	1		32.8	420	1.0	59.8	
	10	68.8	250	1.1	84.3	4		113.2	350	0.9	60.7	
	12	64.5	305	1.0	88.2	5		0	33.5	490	1.0	49.4
	14	105.0	270	1.0	93.7		2	42.2	415	0.9	61.7	
16	103.0	265	0.9	110.2	4		44.7	395	1.1	66.4		
18	136.5	235	1.2	98.8	6		49.0	350	1.1	74.0		
2	0	46.8	485	1.3	54.1	6	0	24.1	495	1.0	48.5	
	2	57.8	480	1.2	58.9		3	33.5	470	1.1	60.7	
	4	57.8	450	0.9	58.9		5	33.9	430	1.1	66.4	
	7	136.5	420	1.8	65.5		7	47.2	430	1.1	69.2	
3	0	51.2	505	0.9	42.8	10	10	125.0	365	1.2	34.8	
	3	29.2	435	0.9	49.4		0	44.7	470	1.0	60.7	
	5	28.5	409	0.9	55.1		2	33.5	340	1.1	55.1	
	7	33.0	310	0.9	61.5		5	139.5	365	1.2	55.1	
	10	50.0	310	1.0	85.2		4	0	29.7	440	1.0	60.7
	12	45.6	330	1.2	75.8			3	30.0	450	0.7	65.5
Group 4 (10 per cent alcohol and 0.6 per cent sodium chloride given, as much as animal would drink)												
1	0	27.0	470	1.0	41.9	3	0	44.7	470	1.0	60.7	
	2	65.2	430	1.1	62.6		2	33.5	340	1.1	55.1	
	4	28.7	485	0.8	40.2		5	139.5	365	1.2	55.1	
	6	40.7	515	1.2	50.4		4	0	29.7	440	1.0	60.7
	8	30.5	520	1.1	59.8	3		30.0	450	0.7	65.5	
	10	33.1	490	1.1	70.2	5		25.2	510	0.9	67.3	
	11	35.9	480	1.0	85.2	7		25.9	500	0.9	66.4	
	2	0	34.3	470	1.0	50.4	11	11	28.0	460	0.9	74.0
2		77.9	410	1.2	65.4	13		76.0	450	1.2	70.6	
6		51.8	495	1.1	62.6	5	0	30.3	500	1.2	44.7	
8		39.9	523	1.1	61.7		3	38.0	500	0.6	55.1	
10		49.0	520	1.0	59.8		5	34.5	510	1.0	53.2	
13		27.3	540	1.0	53.2		7	45.8	555	1.1	52.2	
15		25.8	550	1.2	54.1	6	0	23.9	470	1.0	55.1	
17		28.3	540	1.3	52.2		3	34.5	445	0.9	71.1	
20		32.1	555	1.1	57.0		5	27.5	530	0.9	56.0	
22		31.6	550	0.7	53.2		7	24.2	485	1.0	66.4	
24		29.4	475	0.8	49.4							
27		35.3	545	0.7	53.2							
29	40.6	580	0.9	49.4								

sutures. The animals in this series were divided into two groups of 6 animals each, the first being given tap water only and the second an 0.85 per cent solution of sodium chloride.

Frequent determinations were made of the nonprotein nitrogen and the creatinine content and the carbon dioxide-combining power of the blood and the chloride content of whole blood throughout each experiment. An autopsy was done on each animal. Only those that were free from complications are included in this report.

RESULTS OF EXPERIMENTS

Series 1.—Obstruction of the Jejunum: Group 1 animals, those receiving water only, lived an average of eleven and one-third days. Analysis of the blood showed the typical rise in the nonprotein nitrogen content and the carbon dioxide-combining power and a marked drop in the chloride content. All determination of creatinine gave results within normal limits (table 1).

For group 2 animals, those receiving 0.6 per cent solution of sodium chloride, the average length of life was twenty-six and one-sixth days. Except in 1 animal there was no constant increase in the non-protein nitrogen. The chloride content showed some decrease in 4 of

TABLE 2 (Series 2).—*Obstruction at Pylorus by Section and Suture of Duodenum and Stomach*

Dog No.	Day After Operation	Blood				Dog No.	Day After Operation	Blood			
		Mg. per 100 Ce.			CO ₂ Combining Power, Vol. per Cent			Mg. per 100 Ce.			CO ₂ Combining Power, Vol. per Cent
		Total Non-protein Nitrogen	Chlorides (Whole Blood)	Creatinine				Total Non-protein Nitrogen	Chlorides (Whole Blood)	Creatinine	
Group 1 (water given by mouth as desired)											
1	0	31.4	535	1.3	53.2	3	3	53.3	295	1.3	85.6
	1	30.3	480	1.3	58.9		4	95.0	260	1.4	97.0
	2	30.5	410	1.1	64.5		5	183.0	260	2.0	91.4
	3	55.4	350	1.2	85.2						
	4	103.4	300	1.5	95.0	4	0	28.0	515	1.5	59.8
	5	124.5	250	1.5	102.6		1	33.3	465	1.4	71.1
	6	149.0	180	1.8	132.8		2	51.5	390	1.5	80.6
							4	198.0	245	2.8	95.6
2	0	35.5	490	1.3	48.5						
	1	40.6	460	1.6	59.8	5	0	26.7	513	1.3	50.4
	2	50.8	330	1.4	76.2		1	30.6	505	1.3	52.2
	3	230.0	230	1.4	95.0		2	37.0	400	1.3	71.1
	4	256.0	155	1.8	110.2		3	100.0	285	1.5	87.6
	5	135.0	30	2.0	112.0						
3	0	38.5	560	1.4	44.7	6	0	26.5	535	1.2	40.0
	1	34.5	505	1.3	54.1		1	30.7	485	1.2	50.4
	2	48.7	390	1.4	77.7		2	40.0	395	1.3	71.1
							3	83.3	310	1.4	89.4
Group 2 (0.85 per cent solution of sodium chloride given, as much as animal would drink)											
1	0	31.9	520	1.4	56.1	4	1	31.2	460	1.4	50.4
	1	36.1	475	1.4	57.9		2	69.7	425	1.6	69.2
	2	103.4	495	1.9	57.0		3	145.0	380	1.8	71.6
	3	159.5	425	2.3	65.5		4	204.5	410	2.3	72.1
	4	240.0	460	4.6	60.7						
2	0	32.6	505	1.4	46.6	5	0	37.5	530	1.5	45.7
	1	35.1	460	1.4	69.2		1	38.7	490	1.4	54.1
	2	57.8	455	1.3	62.6		2	64.5	455	1.5	61.7
	3	110.0	480	1.8	57.0		3	98.8	455	1.4	67.3
	4	128.0	485	2.0	61.8		4	167.0	460	1.8	63.6
							5	225.0	450	2.0	78.7
3	0	36.1	530	1.6	48.5		6	151.0	475	1.6	79.6
	1	31.4	490	1.5	58.9		7	263.0	500	2.1	68.3
	2	65.9	415	1.7	80.6						
	3	119.0	390	1.8	78.0	6	0	29.5	460	1.5	50.4
	4	195.0	430	2.4	71.6		1	38.9	425	1.4	76.8
	5	254.0	445	4.2	69.2		2	81.0	380	1.7	74.0
							4	164.7	420	1.9	80.2
							5	203.0	455	3.2	64.5
4	0	30.5	490	1.3	45.7		6	271.0	500	4.1	60.7

the 6 animals, but the change was not marked. There was a rise in the carbon dioxide-combining power in all but 1 animal. There was no change from normal in the creatinine content (table 1).

Group 3 animals, those receiving 10 per cent alcohol, lived an average of twelve and one-sixth days. The blood showed an increase in the nonprotein nitrogen content and the carbon dioxide-combining power and a decrease in the chloride and the normal creatinine content (table 1).

In group 4 of this series, composed of animals receiving 10 per cent alcohol in 0.6 per cent solution of sodium chloride, the average length of life was twelve days. There were an average slight increase in the non-protein nitrogen content of the blood, an increase in the carbon dioxide-combining power in 4 of the animals and a slight decrease in the chloride content in only 2 of the animals. The creatinine content remained within normal limits (table 1).

Series 2.—Obstruction at the Pylorus: Animals of group 1 of this series received water only. The average length of life was four and one-third days. In each animal there was a marked rise in the nonprotein nitrogen content and the carbon dioxide-combining power and a marked drop in the chloride content of the blood; there was a slight terminal rise in the creatinine content in 2 animals (table 2).

Group 2 dogs, those receiving 0.85 per cent solution of sodium chloride, lived an average of five days. The nonprotein nitrogen content showed a much more marked and rapid increase than in any other group in either series. There was a moderate rise in the carbon dioxide-combining power of the blood of each animal. The decrease in chloride content was slight in 5 animals. There was a definite terminal rise in creatinine content in all animals (table 2).

COMMENT

Previous experiments¹ have shown that dogs with an obstruction of the upper part of the jejunum live more than twice as long if permitted to drink water as desired. The experiments here recorded show that animals drinking a dilute solution of sodium chloride live more than twice as long as those drinking tap water. The average chloride content of whole blood was slightly reduced, but to a much smaller degree than in animals drinking water only. The same thing was true of animals with obstruction of both the jejunum and the pylorus. The average length of life for animals receiving 10 per cent alcohol was only approximately one day longer than for those receiving water. The addition of sodium chloride to the alcohol did not increase the length of life. The drinking of alcohol did not prevent the changes in the blood characteristic of high obstruction of the jejunum. When sodium chloride was added to the alcohol, changes were prevented in the nonprotein nitrogen and the chloride content, and there was only a slight average increase in the carbon dioxide-combining power. There was no increase in creatinine content in any group of series 1.

In series 2, with pyloric obstruction the length of life was not significantly increased by the giving of sodium chloride. It is interesting to note the great difference in the changes in nonprotein nitrogen in animals with jejunal obstruction and with obstruction at the pylorus. In the

latter the nonprotein nitrogen increased steadily until death, whereas in the former either there was no change or the average increase was small. The increase in nonprotein nitrogen was greater in animals receiving sodium chloride than in those receiving water, although the average chloride content of the blood in the former remained within normal limits. The group with pyloric obstruction which received sodium chloride showed the only constant increase in creatinine content in both series.

From these experiments it is evident that sodium chloride was absorbed from the upper part of the intestine and the stomach in cases of jejunal and of pyloric obstruction. Previous experiments indicate that life is prolonged by giving water *ad libitum* in cases in which the upper part of the jejunum is obstructed. In the present experiments duration of life was more than doubled when sodium chloride was given by mouth to animals with jejunal obstructions 25 cm. below the ligament of Treitz.

All animals of both series lost weight rapidly. The total loss of weight was in direct proportion to the duration of life.

CONCLUSIONS

A series of experiments on dogs with jejunal obstruction and a second series, on dogs with pyloric obstruction, are presented. In the first series, solution of sodium chloride, alcohol and a combination of solution of sodium chloride and alcohol, and in the second series, water and solution of sodium chloride were given orally, to determine their effect on the length of life and on the chemical character of the blood and the absorbability of sodium chloride in cases of obstruction, of the upper part of the bowel and of the stomach, respectively.

The life span of dogs with jejunal obstruction was more than doubled when they received sodium chloride rather than water only.

Sodium chloride when given by mouth to animals with experimental jejunal obstruction was absorbed in sufficient quantity to maintain the chloride content of the blood at an average level just below normal. When water alone was given, there was a marked and constant decrease in the chloride content.

Alcohol and a combination of alcohol and sodium chloride when given by mouth did not appreciably lengthen the life of the animals. In the group receiving the added sodium chloride chemical changes in the blood characteristic of untreated jejunal obstruction were prevented.

In dogs with pyloric obstruction the drinking of solution of sodium chloride produced a greater increase in the nonprotein nitrogen content than did the drinking of water. This is in direct contrast to the effect

of sodium chloride on dogs with jejunal obstruction. The chloride content of the blood showed only a slight decrease below normal when sodium chloride was given, as compared with a marked decrease when water was taken. The typical increase in the carbon dioxide-combining power was evident in dogs receiving water, but there was only a slight increase when sodium chloride was given. The constant increase in creatinine content in dogs receiving sodium chloride was striking, since it did not occur in any other group. The rise in the nonprotein nitrogen and in the creatinine content in dogs with pyloric obstruction which were given sodium chloride by mouth indicated that sodium chloride did not offer the same protection against these changes in animals with this type of obstruction as in those with obstruction of the jejunum.

LEUKOCYTE EXHAUSTION FOLLOWING SURGICAL PROCEDURES

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It is often baffling to the surgeon when after an operation a patient takes an unexplained turn for the worse or follows a progressively downhill course without apparent reason. I have recently observed that in association with such a course examination of the blood frequently shows leukopenia, with a normal differential count and a marked shift to the left of the neutrophils. This picture signifies a wearing out of the leukopoietic power and offers an explanation of the patient's lack of response to ordinary measures. This leukocyte exhaustion always indicates a serious prognosis and is probably more common than is generally realized. It therefore, I believe, deserves more recognition as a complication following surgical procedures.

Leukocyte exhaustion was first described by Turk¹ in 1907 and is usually considered as due to the "overwhelming irritation" of severe sepsis (Schilling²) or to "long continued infection as the result of a persistent drain" (Piney³). The bone marrow is usually hyperplastic, with an abnormally large number of myeloblasts and immature neutrophils. Gelatinous degeneration and a picture of almost complete aplasia may also occur.³ Whether the damage, however, is primarily to the bone marrow or to some earlier link in the hemopoietic chain is not as yet known.

I shall present 7 cases in which leukocyte exhaustion occurred. In all there was the characteristic leukopenia, with a marked shift to the left of the neutrophils. In more than half of the cases the degree of sepsis did not appear sufficient to have exhausted a normal leukopoietic power. It may be assumed, therefore, that in these cases the leukocyte reserve was at an abnormally low level before operation. The term "low leukocyte reserve" will be used to designate this condition and to

1. Turk, W.: *Septische Erkrankungen bei Verkümmerng des Granulozytensystems*, Wien. klin. Wchnschr. **20**:157 (Feb. 7) 1907.

2. Schilling, V.: *The Blood Picture and Its Clinical Significance*, St. Louis. C. V. Mosby Company, 1929, pp. 149-154 and 180.

3. Piney, A.: *Recent Advances in Hematology*, Philadelphia, P. Blakiston's Son & Co., 1931, pp. 146 and 162.

differentiate it from Doan's⁴ "low marrow reserve," in which agranulocytosis rather than leukocyte exhaustion develops.

I have separated the cases into two groups, depending on whether the leukocyte reserve is considered to have been normal or low. In group 1 are 3 cases in which overwhelming or prolonged sepsis was necessary to cause the exhaustion, i. e., cases in which there was a normal leukocyte reserve. In group 2 are 4 cases in which the same picture was brought about by a lesser degree of strain, i. e., cases in which there was a low leukocyte reserve.

GROUP 1: LEUKOCYTE EXHAUSTION IN CASES IN WHICH THERE WAS A NORMAL RESERVE

CASE 1.—J. H., a man aged 33, was admitted to the Crouse-Irving Hospital on July 6, 1937, with severe abdominal pain of three days' duration. The onset of the severe pain had been sudden, and aside from some abdominal discomfort during the previous week the past history was not significant.

TABLE 1.—*Blood Counts in Case 1*

Date	Leuko- cytes	Neutro- phils, per Cent	Lympho- cytes, per Cent	Mono- cytes, per Cent	Nonfilamented Neutrophils, per Cent*	Comment
7/7	4,950	78	21	1	88	Liver extract (twice)
7/8	6,100	93	7	0	89	Liver extract (twice)
7/9	15,650	74	26	0	80	Terminal count

* Figures indicate percentage of total number of neutrophils.

Directly after admission a laparotomy was performed, but the patient's condition was so precarious that the exploration was interrupted and the abdomen closed with drainage. Later in the day cyanosis developed, and evidence of bronchopneumonia was present at the bases of both lungs. In spite of supportive measures, the downhill course continued, and death occurred on the morning of the third postoperative day.

A blood count on the day after operation showed the characteristic picture of leukocyte exhaustion. The total count was 4,950 per cubic millimeter, with 78 per cent neutrophils, 88 per cent of which were nonfilamented (table 1). Four injections of 3 cc. liver extract (concentrated) were given, but because of the rapidity of the downhill course, I shall attempt no interpretation of the results of therapy.

Neeropsy revealed a perforated duodenal ulcer on the anterior surface of the duodenum, acute generalized fibrinous peritonitis and bilateral bronchopneumonia. Smears from the rib marrow showed marked hyperplasia of the myeloblasts, with few adult cells and even myelocytes.

Comment.—In this case there was no reason to suppose that the leukocyte reserve was abnormal before operation, the degree of sepsis having been sufficiently severe to account for an "overwhelming" of the hemopoietic system. Not only was generalized peritonitis present for probably three full days, but there had been an abdominal operation and beginning pneumonia.

4. Doan, C. A.: The Neutropenic State: Its Significance and Therapeutic Rationale, J. A. M. A. 99:194 (July 16) 1932.

CASE 2.—N. R., a man aged 44, was admitted to the Hospital of the Good Shepherd, Syracuse University, on April 23, 1934, because of the recurrence of an appendical abscess. Six months before, the abscess had been opened and drained. The leukocyte response at that time was apparently adequate, and convalescence progressed satisfactorily.

Two weeks after admission a fistulous tract was excised and a large amount of pus drained from the right colic gutter and cecal area. In spite of this, the temperature continued elevated for over three weeks before finally falling to normal. Seven weeks later the temperature again rose, and after five weeks of almost continual fever an extensive lumbar abscess was opened and drained. The fever persisted, however, and when leukocyte counts were next taken, on September 5 and September 11 (table 2), a picture of leukocyte exhaustion had developed.

From this time on the patient began to lose ground even more rapidly, and his weakness finally became so alarming that a blood transfusion was given. After a period of temporary improvement, during which the leukopenia con-

TABLE 2.—*Blood Counts in Case 2*

Date	Leuko- cytes	Neutro- phils, per Cent	Lympho- cytes, per Cent	Mono- cytes, per Cent	Eosino- phils, per Cent	Baso- phils, per Cent	Nonfilamented Neutrophils, per Cent	Comment
4/25	12,000	80	17	3	0	0	18	
5/ 4	Recurrent appendical abscess drained
5/ 7	7,600	80	14	4	2	0	..	
8/ 6	14,300	78	16	6	0	0	..	
8/14	Lumbar abscess drained
9/ 5	4,400	57	27	13	3	0	..	
9/11	4,200	53	46	0	1	0	87	
9/16	Blood transfusion
9/18	3,200	61	32	6	1	0	41	
9/20	Administration of powdered liver started
9/21	5,500	58	30	10	1	1	55	
9/24	6,300	63	37	0	0	0	..	
9/30	5,100	51	44	5	0	0	51	

tinued though the percentage of immature forms was lower (September 18, table 2), the temperature again became elevated. This time administration of powdered liver extract in doses of 1 drachm (3.88 Gm.) twice daily was started and continued until the patient was discharged. In two days the temperature was again normal and continued so. The leukopenia promptly disappeared, and the percentage of stab neutrophils remained only moderately elevated. The general condition improved rapidly, and the patient was discharged from the hospital on October 23, just six months after admission.

Comment.—The blame for the leukocyte exhaustion in this case can certainly be placed on "long continued infection as the result of a persistent drain." Except for approximately six weeks between operations, the temperature was elevated daily for over five months. The leukocyte picture at the time of admission shows an adequate reaction as regards both the total count and the maturity of the neutrophils (table 2), which is added evidence that the breakdown occurred in a previously healthy hemopoietic system.

CASE 3.—H. N., a woman aged 23, was admitted to the Hospital of the Good Shepherd, Syracuse University, on Aug. 8, 1934, with diarrhea and intermittent pain in the lower part of the abdomen of four days' duration. Because of

indefinite abdominal findings and a history of drinking well water, the patient was suspected of having typhoid and was treated accordingly. Six days later, however, signs of peritonitis developed, and at operation a ruptured appendix was removed and the abdomen drained.

For the first week postoperatively the patient did well, the temperature falling from 104 F. to nearly normal and the purulent discharge from the wound decreasing. During the next two weeks, however, the condition became progressively worse, with the temperature steadily rising and the profuse discharge from the abdomen continuing. On the eighteenth postoperative day exploration for a suspected subphrenic abscess was unsuccessful, and three days later the patient died. Three blood transfusions were of only transitory benefit.

Three leukocyte counts were taken. The first two showed a satisfactory number of leukocytes, but the final count, with leukopenia and a marked neutrophilic shift to the left, presented the characteristic picture of leukocyte exhaustion (table 3).

Necropsy was not performed.

Comment.—This patient suffered continually for about thirty-two days from rather severe sepsis. First there had been appendicitis, next peritonitis and finally an infection at the operative wound and a draining abdominal sinus. By the time the last complications set in the leukopoietic power had become exhausted.

TABLE 3.—*Blood Counts in Case 3*

Date	Leuko- cytes	Neutro- phils, per Cent	Lympho- cytes, per Cent	Mono- cytes, per Cent	Nonfilamented Neutrophils, per Cent	Comment
8/ 8	13,300	80	9	1	...	
8/13	19,000	84	14	2	...	
9/ 4	4,600	80	20	0	100	Nine hours before death

Consideration of the severity of the strain and the apparent adequacy of leukocytes at the first two counts suggests the probability that a normal leukocyte reserve was present at the time of admission.

A special point in this case is that more frequent blood counts might have indicated a beginning failure at an early enough time for the administration of liver extract and blood transfusions to have proved effective.

GROUP 2: LEUKOCYTE EXHAUSTION IN CASES IN WHICH THERE WAS LOW RESERVE

CASE 4.—C. G., a man aged 44, was admitted to the Hospital of the Good Shepherd, Syracuse University, on Oct. 18, 1934, with severe pain in the lower part of the abdomen associated with vomiting and diarrhea of two weeks' duration. The illness had begun suddenly with the abdominal pain.

The patient had had typhoid fever twenty-eight years before and malaria and dysentery since that time. There had been three previous admissions. The first, six years before, had been for ischiorectal abscess, and the second, four years before, for a recurrence of the dysentery. On both occasions blood counts had shown adequate leukocytes. At the time of the third admission, two years before, the patient had been acutely ill with cholecystitis of twelve hours' duration. He was treated conservatively for three weeks, after which time an infected gallbladder was removed and a contiguous hepatic abscess drained. The interesting point in connection with this admission is that a blood count only two days

after the onset of the acute illness showed leukopenia (3,500 white blood cells, 78 per cent polymorphonuclears, 15 per cent lymphocytes and 7 per cent mononuclears). The leukopenia disappeared, however, during the interval and did not reappear either before or after the operation.

When admitted in 1934, the patient was in such poor condition that an operation was not attempted. The course was steadily downhill, and death occurred eleven days later. Table 4 clearly shows the exhaustion of leukopoiesis, a leukopenia with marked shift to the left persisting until the final count, one hour before death. One blood transfusion was given ten hours before death.

At necropsy a perforated ulcer of the cecum, acute colitis, generalized peritonitis and pulmonary congestion and edema were observed. The microscopic diagnosis was acute splenic tumor, central necrosis and fatty changes in the liver, toxic changes in the kidneys and ulcerative undermining colitis, apparently due to amebic infection. Studies of bone marrow were not made.

Comment.—I do not know, of course, how long before admission the picture of leukocyte exhaustion had been present. The cecal ulcer had undoubtedly perforated two weeks before, and peritonitis of such duration certainly constitutes an "overwhelming irritation." Two years before, however, leukopenia had been present during an attack of cholecystitis, suggesting that a low leukocyte reserve

TABLE 4.—*Blood Counts in Case 4*

Date	Leuko- cytes	Neutro- phils, per Cent	Lympho- cytes, per Cent	Mono- cytes, per Cent	Eosino- phils, per Cent	Nonfilamented Neutrophils, per Cent	Comment
10/19	4,000	70	29	0	1	97	
10/23	3,000	60	33	5	2	93	
10/26	4,200	67	30	3	0	..	
10/28	
10/29	12,000	67	31	2	0	91	Blood transfusion Count taken one hour before death

existed at that time. It is probable, therefore, that the leukopoietic function was still subnormal at the onset of the present illness.

It may be that in this case the many serious illnesses extending back for twenty-eight years resulted in a permanent impairment of the leukocyte reserve.

CASE 5.—B. F., a man aged 67, was admitted to the Hospital of the Good Shepherd, Syracuse University, on April 8, 1935, with severe abdominal pain, which had begun suddenly five hours before. Throughout the previous year the patient had noticed that his stools were getting smaller and occurring at more frequent intervals than usual.

The patient was found to have an annular carcinoma of the rectum, but because of the seriousness of his general condition operation was not considered. Thirty-six hours after being admitted he died. The blood count showed a typical picture of leukocyte exhaustion (table 5).

At necropsy the anatomic diagnosis was carcinoma of the rectum, perforation of the large intestine, generalized peritonitis and generalized arteriosclerosis. The significant microscopic observations were rather marked pigmentation of the liver and the spleen and rather marked hyperplasia of the bone marrow, with some apparent hemorrhage and a few adult cells of the myeloblastic series.

Comment.—The amount of strain required to bring about leukocyte exhaustion in this case was apparently small. The first blood count was taken one hour after admission, so that only six hours had elapsed since the rupture of the ulcer and

the beginning of peritonitis. Just what part the carcinoma played either in producing toxicity or in causing malnutrition can only be speculated on. Whatever the cause, the leukopoietic power of this patient must have been markedly impaired before the rupture of the ulcer. The peritonitis itself in that short time could have acted only as a "last straw."

CASE 6.—H. S., a woman aged 33 years, was admitted to the Syracuse Memorial Hospital on June 20, 1934, with symptoms of acute appendicitis. She had had four normal pregnancies, the last one six years before.

At operation bilateral acute salpingitis was found. The abdominal contents were not disturbed, and the wound was closed without drainage. At first the patient did well, but on the second postoperative day there were marked abdominal distention and vomiting. Although a blood count at the time of admission had shown an adequate number of leukocytes, one taken at this time showed the characteristic picture of leukocyte exhaustion (table 6).

TABLE 5.—Blood Counts in Case 5

Date	Leukocytes	Neutrophils, per Cent	Lympho- cytes, per Cent	Monoeytes, per Cent	Nonflamented Neutrophils, per Cent
4/8 a.m.	2,100				
4/8 p.m.	3,600	70	24	6	93

TABLE 6.—Blood Counts in Case 6

Date	Leuko- cytes	Neutro- phils, per Cent	Lympho- cytes and Monoeytes, per Cent	Eosino- phils, per Cent	Baso- phils, per Cent	Nonfla- mented Neutrophils, per Cent	Comment
6/20	16,400	94	6	0	0	..	Admission
6/21	Operation
6/22	3,000	82	18	0	0	73	Liver extract and blood transfusion given
6/23	3,200	67	32	1	0	89	
6/24	3,500	65	35	0	0	74	Liver extract
6/25	5,500	72	28	0	0	53	Liver extract
6/26	6,800	82	16	2	0	37	
6/28	10,200	70	20	1	0	37	
7/ 6	5,300	57	41	2	0	39	
7/11	6,800	53	42	4	1	38	Discharge

One dose of 3 cc. of liver extract (concentrated) was given and followed by a blood transfusion. By the morning of the next day the distention had subsided, and recovery continued uneventfully. The picture of exhaustion persisted for several days, a return of the blood count to normal following two more injections of liver extract (table 6). Between the time of the operation and the next leukocyte count 30 cc. of a derivative of sulfanilamide known as prontosil (the disodium salt of 4-sulfamidophenyl-2'-azo-7'-acetyl-amino-1'-hydroxy-naphthalene-3',6'-disulfonic acid) and 45 grains (2.91 Gm.) of sulfanilamide had been administered. With the discovery of leukocyte exhaustion, however, this treatment was discontinued.

Comment.—The initial response to the salpingitis and the localized peritonitis seemed to have been entirely adequate, but the added strain of the abdominal operation was apparently too great for the hemopoietic system. The use of sulfanilamide and its derivatives is not considered a factor in leukocyte exhaustion, the only white cell dyscrasia as yet reported following such medication being

agranulocytosis.⁵ It is probable, then, that a low leukocyte reserve existed prior to the onset of the present illness and that in this case the "last straw" was the operation.

CASE 7.—K. B., a woman aged 34 years, was admitted to the Syracuse Memorial Hospital on Jan. 3, 1936, for her second delivery. Her first pregnancy, four years before, had been complicated by influenza and bilateral otitis media and the puerperium by a mastoiditis requiring mastoidectomy. The leukocyte count on the first day post partum had shown an adequate number of leukocytes (15,700, with 87 per cent polymorphonuclears), but at the time of the mastoidectomy, one month later, the count had been only 6,500 per cubic millimeter, with 59 per cent polymorphonuclears.

The second pregnancy and delivery were uneventful. On the third day post partum, however, the abdomen became distended, and vomiting began. The distention continued to increase until four days later, when peristaltic waves were observed, and a laparotomy was performed. At operation the colon was found to be greatly distended as far as the splenic flexure, and the angulation at that

TABLE 7.—*Blood Counts in Case 7*

Date	Leuko- cytes	Neutro- phils, per Cent	Lympho- cytes and Monocytes, per Cent	Eosino- phils, per Cent	Baso- phils, per Cent	Nonfila- mented Neutrophils, per Cent	Comment
1/ 4	7,000	71	26	3	0	..	First day post partum
1/10	3,500	74	23	3	0	91	Operation; liver extract given
1/11	4,300	70	29	1	0	87	Liver extract given
1/12	5,900	74	25	1	0	51	
1/13	6,700	80	18	2	0	43	Liver extract given
1/14	7,100	72	25	3	0	26	
1/15	7,200	74	24	2	0	28	Liver extract given
1/16	7,000	68	30	2	0	43	
1/17	8,300	68	29	3	0	28	Liver extract given
1/18	6,900	66	34	0	0	29	
1/19	5,900	61	35	4	0	16	Liver extract given
1/20	5,300	55	40	5	0	31	
1/25	12,400	90	8	2	0	58	Menses start
1/26	4,300	61	38	1	0	10	Liver extract given
1/27	4,100	40	56	1	3	20	
1/28	4,300	43	48	6	3	16	

point was apparently the reason for the mechanical symptoms. An appendicostomy was the only procedure undertaken and the abdomen was closed without drainage.

The leukocyte count just before operation showed a typical picture of exhaustion. The total count was 3,500 per cubic millimeter, with 74 per cent polymorphonuclears, 91 per cent of which were nonfilamented forms (table 7). Intramuscular injections of liver extract (concentrated) were begun immediately and given in doses of 3 cc. every two days for three doses.

After operation and the beginning of liver therapy the patient improved rapidly. As the distention subsided, the leukocyte count rose and the percentage of immature forms fell (table 7). Recovery was thereafter uneventful, except for a temporary recurrence of distention which coincided with the strain of premenstrual leukocytic infiltration of the uterus.⁶

An increase in the neutrophilic shift to the left was again present, though this time associated with leukocytosis instead of leukopenia (table 7). Liver

5. Borst, J. G. G.: Death from Agranulocytosis After Treatment with Prontosil Flavum, *Lancet* 1:1519 (June 26) 1937.

6. Novak, E., and Telinde, R. W.: The Endometrium of the Menstruating Uterus, *J. A. M. A.* 83:900 (Sept. 20) 1924.

therapy was again followed by a disappearance of the distention and a return of the leukocyte count to normal. It should be noted, however, that the premenstrual strain itself is only transitory. Nine days after the recurrence of distention the patient was discharged.

Comment.—In this case it apparently required only the demands of a normal delivery preceded by a normal pregnancy to bring on the picture of leukocyte exhaustion. This means that even at the time of the patient's admission to the hospital the leukocyte reserve was probably low. It should be recalled that during the acute mastoiditis which followed the previous delivery there were only 6,500 leukocytes per cubic millimeter—obviously an inadequate number. This suggests that a low leukocyte reserve had been present four years before.

GENERAL COMMENT

This series of cases illustrates not only the importance of leukocyte exhaustion as a complication following surgical procedures, but the possibility of its occurrence when least expected, the latter point being illustrated by the extreme variability in the degree of strain required to bring it about. On the one hand, overwhelming sepsis may be necessary, as in case 1, and on the other, merely the strain of a normal delivery, as in case 7.

Five cases have been reported recently, 2 by Rosenthal⁷ and 3 by Rosenthal and Kugel,⁸ in which this blood picture was observed. The condition was named "hypoleukocytic angina" to distinguish it from agranulocytic angina. In 2 cases (case 11⁷ and case 2⁸) the exhaustion developed spontaneously, illustrating a complete lack of leukocyte reserve. In the other 3 (case 12⁷ and cases 1 and 3⁸), it followed military tuberculosis, an abdominal operation and streptococcal laryngitis, respectively.

Leukocyte exhaustion, then, has already been recognized, as it occurs not only in cases of severe or prolonged sepsis but in cases of much milder strain and even in cases in which there is no strain at all. My aim is to emphasize to the surgeon the importance of keeping it in mind as a possible complication of any degree of surgical strain and of discovering its presence early. This means: (1) that leukocyte counts should be made at the time of admission and especially before operation for the detection of any immediate abnormality and for possible future comparisons; (2) that counts should be made every day or two when severe sepsis is present, in order to detect leukocyte exhaustion at an early stage; (3) that they should be made whenever a patient's condition takes an unexplained turn for the worse, especially postoperatively and in the presence of abdominal distention, even in

7. Rosenthal, N.: Hematological Aspects of Agranulocytosis and Other Diseases Accompanied by Extreme Leukopenia, *Am. J. Clin. Path.* **1**:7 (Jan.) 1931.

8. Rosenthal, N., and Kugel, M. A.: Hypoleukocytic Angina: An Unusual Form of Infectious Leucopenia, *J. Lab. & Clin. Med.* **19**:344 (Jan.) 1934.

the absence of demonstrable infection. The percentages of non-filamented neutrophils should, of course, be determined at every count.

The steps in the process of leukocyte exhaustion are, according to Schilling,² as follows: First, there is the leukocytosis with neutrophilia and increasing shift to the left. With continued irritation the shift to the left becomes more marked; myelocytes appear, and the total count falls even to the point of leukopenia. If the sepsis is of long standing, the shift may be "degenerative" rather than "regenerative"—that is, show a great increase of stabnuclears without young forms. In the cases reported no attempt has been made to differentiate the "regenerative" from the "degenerative" shifts.

In both case 6 and case 7 it is interesting to note that a paralytic type of abdominal distention was associated with a picture of leukocyte exhaustion. In each case relief of the distention coincided with or was followed by a return of the blood picture to normal. This suggests that a possible relation exists between a low leukocyte reserve and a low threshold for paralytic ileus.

The treatment of leukocyte exhaustion should probably be the same whether a severe or a mild strain is required to bring it about. In the cases reported, administration of liver extract, both orally and intramuscularly, and blood transfusions appeared to be of great value if administered early enough in the course of the leukopoietic breakdown.

CONCLUSIONS

1. Leukocyte exhaustion (leukopenia with marked neutrophilic shift to the left) is an important complication following surgical procedures because of its apparent frequency and the seriousness of the prognosis.

2. Leukocyte exhaustion is usually associated with overwhelming or prolonged sepsis but may occur after mild strain, in which case a low leukocyte reserve may be assumed to have existed.

3. There appears to be a relation between leukocyte exhaustion in patients with extremely low leukocyte reserve and paralytic abdominal distention.

4. The administration of liver extract and blood transfusions appear to be effective therapeutic measures for combating leukocyte exhaustion if undertaken early and if sepsis is not too severe.

EXPERIMENTAL ADMINISTRATION OF DUODENAL CONTENTS TO DOGS WITH ACUTE HIGH INTESTINAL OBSTRUCTION

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Attention has been called repeatedly to the similarity between the symptoms of acute high intestinal obstruction and those of duodenal fistula. Without going into a detailed review of theories as to the cause of death after high intestinal obstruction, we may say that considerable evidence has been presented that the loss of the contents of the upper part of the intestine by vomiting is a most important, or the most important, factor. The fact that dogs with a duodenal fistula suffer a rapid drop in blood chlorides, dehydration, rise of carbon dioxide-combining power and death within a few days, as shown by Eisberg¹ and by one of us,² strongly suggests that the loss of duodenal fluid by vomiting is of prime significance.

Although the loss of pancreatic juice alone produces symptoms the same as or similar to those enumerated above, it cannot be stated as yet that this loss of pancreatic juice is the sole cause of the symptoms produced by duodenal fistula. As pointed out by Draper Maury³ in 1910, when an intestinal obstruction is produced in dogs above the level of the bile and pancreatic ducts the animals live for a considerable time; but when the obstruction is below this level the period of survival is only a few days. Draper also showed that if the bile duct was transplanted below the level of the obstruction there was no difference in the outcome; but when the pancreatic ducts were transplanted below the level of the obstruction "a large proportion" of the dogs lived.

From the Department of Experimental Surgery of the Creighton University School of Medicine.

1. Eisberg, H. B.: Experimental Intestinal Obstruction, *Ann. Surg.* **74**: 584, 1921.

2. Hill, F. C.; Neigus, I., and Wilhelmj, C. M.: Method of Preparing Duodenal Pouches for Use in Experimental Work, *J. Lab. & Clin. Med.* **19**: 1126, 1934.

3. Draper Maury, J. W.: Death in Acute Intestinal Obstruction and Kindred Conditions Is Due to Physiologic Disturbance, *J. A. M. A.* **54**: 5 (Jan. 1) 1910.

Jenkins⁴ drained the duodenum and upper part of the jejunum into the ileum and anastomosed another portion of jejunum, the lower end of which was obstructed, to the stomach. The obstructed part thus consisted of stomach and a length of jejunum which had been connected to the stomach, and the duodenal contents were drained into the ileum and not lost. He found that the dogs lived from twelve to thirty-three days, suffered a gradual loss of weight, vomited occasionally and showed a gradual fall in blood chlorides and a gradual rise in carbon dioxide-combining power. After similar transplantation of the duodenum by Eisberg and Draper⁵ the dogs lived seventeen days, as compared to six days with a simple high obstruction.

Morton and Pearse⁶ stated that in several operations on their patients, they performed an anastomosis between obstructed and collapsed loops of bowel, diverting the contents around the obstruction, and obtained favorable results. Hartwell, Hoguet and Beekman⁷ and Haden and Orr⁸ showed that in simple high intestinal obstruction in dogs life can be prolonged to as long as a month by the administration of sodium chloride. McIver and Gamble⁹ and others expressed the belief that in simple obstruction the symptoms are due to gradual dehydration and to disturbance of the acid-base equilibrium. Evidence has also been produced by Elman and Hartman¹⁰ that the loss of pancreatic juice causes death by dehydration and by the loss of base bicarbonate, and they have shown that life in such dogs is prolonged by the administration of a physiologic solution of sodium, potassium and calcium chloride. Jenkins,¹¹ who found that in dogs with a transplanted

4. Jenkins, H. P.: Experimental Ileus: I. High Obstruction with the Biliary, Pancreatic and Duodenal Secretions Shortcircuited Below the Obstructed Point, *Arch. Surg.* **19**: 1072 (Dec.) 1929.

5. Eisberg, H. B., and Draper, J. W.: Intestinal Obstruction, *J. A. M. A.* **71**: 1634 (Nov. 16) 1918.

6. Morton, J. J., and Pearse, H. E.: Similarity in the Effect of Experimental High Intestinal Obstruction and High Complete Intestinal Fistula, *Ann. Surg.* **94**: 263, 1931.

7. Hartwell, J. A.; Hoguet, J. P., and Beekman, F.: An Experimental Study of Intestinal Obstruction, *Arch. Int. Med.* **13**: 701 (May) 1914.

8. Haden, R. L., and Orr, T. G.: Obstruction of the Jejunum: The Effect of Sodium Chlorid on the Chemical Changes in the Blood of the Dog, *Arch. Surg.* **11**: 859 (Dec.) 1925.

9. McIver, M., and Gamble, I. L.: Body Fluid Changes Due to Upper Intestinal Changes, *J. A. M. A.* **91**: 1589 (Nov. 24) 1928.

10. Elman, R., and Hartman, A. F.: Cause of Death Following the Rapidly Total Loss of Pancreatic Juice, *Arch. Surg.* **20**: 333 (Feb.) 1930.

11. Jenkins, H. P.: Experimental Ileus: II. High Obstruction with the Biliary, Pancreatic and Duodenal Secretions, Along with Food and Sodium Chloride Entering the Bowel Below the Obstructed Point, *Arch. Surg.* **25**: 849 (Nov.) 1932.

duodenum there developed a low chloride content of the blood and a high carbon dioxide-combining power, demonstrated that if in addition to the previously described operation the dogs were fed milk, cream and sodium chloride through an enterostomy opening this change in blood chemistry did not occur. These dogs lived from four days to five weeks and showed only gradual loss of weight.

In spite of the fact that the giving of chloride intravenously produces such remarkable results in prolonging the lives of dogs with high intestinal obstruction, thus far, unfortunately, no such pronounced effect has been observed in the mortality rate of human patients similarly treated. It seems evident that for human beings, at least, some other measure of treatment must be evolved.

A somewhat different approach to the problem was suggested by White and Fender¹² when they collected the vomitus from dogs with high intestinal obstruction and injected it below the obstruction through an enterostomy opening. They used only 2 dogs, 1 of which lived a month and the other two weeks. No signs of toxemia developed.

EXPERIMENTS

Because there are certain difficulties which arise when one attempts to collect vomitus from dogs and which will be mentioned later, we have chosen what we believe to be a more direct approach to the problem.

We have introduced duodenal contents into the intestine below the level of a high obstruction in a series of dogs, in order to determine the importance of duodenal juices in prolonging life. A total of 12 dogs was used, 4 of which served as controls. In all the animals an enterostomy was performed by dividing the duodenum below the lower pancreatic duct, bringing out the distal end and closing the proximal end by inversion and suture. The duodenal contents were obtained from additional dogs used as donors, by performing gastrostomy and passing a duodenal tube through the opening into the duodenum. These dogs were trained to lie quietly on a table for hours at a time, and in most cases a fairly free flow of duodenal juices could be obtained, particularly if a small amount of tenth-normal hydrochloric acid was injected through the duodenal tube from time to time.

Of the 4 control animals, 2 received from 600 to 800 cc. of physiologic solution of sodium chloride a day by hypodermoclysis, 1 received 300 cc. of this solution through the enterostomy opening and 1 received no fluid. The duration of life was from two to seven days with an average of four and three-fourths days, the dog which lived longest being the one which received no fluid. The other 8 animals received from 250 to 300 cc. of duodenal juice a day through the

12. White, J. C., and Fender, F. A.: Cause of Death in Uncomplicated High Intestinal Obstruction: The Experimental Evidence to Show That Death Is Due Not to Toxemia, But to the Loss of Digestive Fluids and Salts, *Arch. Surg.* 20: 897 (June) 1930.

enterostomy opening, and 600 to 800 cc. of physiologic solution of sodium chloride was administered by hypodermoclysis. These dogs lived from two to thirteen days, with an average of four and one-half days. Vomiting occurred in only 2 cases among the 12 dogs, and in these was only occasional and the amount of vomitus was small. Of the entire series of dogs, death was due to peritonitis in 3. In all the others no gross pathologic conditions could be demonstrated except that the intestine distal to the obstruction was contracted and there was considerable fluid in the stomach.

Because of the negative results of these experiments, another series of 6 dogs was used. In these animals 350 to 400 cc. of the duodenal contents of freshly killed hogs was injected daily through the enterostomy opening. No injections of saline solution were given in this series. The animals lived from two to four days, with an average of three days, and the observations were negative at necropsy in all dogs except 1, which probably had early peritonitis.

COMMENT

In considering the data which we have obtained we note two striking features: The first is that although physiologic solution of sodium chloride was given in reasonable amounts the lives of these dogs were not conspicuously prolonged. The animals differed from those of previous investigators in having an enterostomy opening in addition to an obstruction. However, because the duodenum was obstructed above this opening there was no possibility that the contents of the upper part of the duodenum would be lost. In addition, the fistula was of the nonleaking type, being so connected that peristalsis would tend to prevent leakage from it. One would not have expected this to affect materially the duration of life. The second rather surprising feature was the fact that vomiting occurred so seldom. In man the most conspicuous feature of an obstruction which has been present for several hours is vomiting—profuse, frequent and stercoraceous. In our dogs vomiting was rare, and never did it approach the human type. It is evident, then, that any attempt to use vomitus in the therapy of obstruction is attended by no inconsiderable difficulty.

CONCLUSIONS

From the experiments conducted we believe the following conclusions may be drawn:

1. Duodenal content administered to dogs through an enterostomy opening below the level of a high intestinal obstruction is not effective in prolonging life.

2. Physiologic solution of sodium chloride administered by hypodermoclysis to dogs with duodenal obstruction and an enterostomy opening does not prolong life.

3. In dogs with duodenal obstruction if nothing is given by mouth vomiting occurs only rarely.

4. The average duration of life with duodenal obstruction and enterostomy is a little over four days, and at necropsy gross examination yields no indication of the cause of death.

LINGUAL THYROID

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Of the developmental anomalies of the thyroid gland, lingual thyroid is the most unusual and the most interesting. It has rarely been the privilege of one person to observe more than a few cases in a lifetime. Clute¹ mentioned but 2 cases in a series of over 8,500 cases of thyroid disease. There was incentive, therefore, for reviewing the subject after I encountered the following remarkable case:

REPORT OF CASE

A 39 year old spinster was admitted to the surgical ward on March 30, 1936, because of a tumor at the base of the tongue. Her family history and past history were not remarkable. She had always had good health until at the age of 37 menorrhagia from uterine myomas developed. Hysterectomy and unilateral oophorectomy had been performed in June 1935.

She consulted her physician in December 1934 about menorrhagia, and routine physical examination revealed a tumor at the base of the tongue. When her slightly thick nasal speech was pointed out, she stated that this might have been coming on for some years and that she had given it little attention. However, she recalled that when she was 28 her throat had been carefully examined after a fishbone had lodged there and that nothing had been said then of any abnormality of the throat or the tongue.

Outpatient Record.—In February 1935 the tumor at the base of the tongue was observed to be smooth, firm, nonmovable on the tongue and nontender. It extended across the width of the tongue and when the tongue was pulled forward largely filled the pharyngeal orifice (fig. 1). At that time a diagnosis of malignant tumor of the tongue was made, although aberrant thyroid was mentioned as a possibility. There were no symptoms or signs of hyperthyroidism or hypothyroidism, and the basal metabolic rate was —3 per cent.

During April 1935 roentgen therapy (3,360 r) was given to the tumor, and this was followed by a slight but definite decrease in its size.

In August 1935 three gold radon seeds (1.7 millicurie each) were introduced into the substance of the tumor. Six weeks later there was some local reaction, evidenced by fibrinous exudate over the tumor and by enlarged tender submandibular nodes.

In January 1936 administration of iodine (syrup of hydriodic acid) was started and continued for six weeks; there was no obvious effect on the tumor. The patient began to have a disagreeable taste, and the breath became foul. A small

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1. Clute, H. M., in discussion on Miller, R. H.: Lingual Goiter, New England J. Med. 208:480, 1933.

necrosing point appeared on the surface of the tumor, and a probe could be passed deeply into the tumor through this point. Presumably there was a central slough resulting from the radon, and this was draining into the mouth.

Admission to Hospital (March 30, 1936).—The patient's only complaint at the time of admission was the disagreeable taste. She admitted that her tongue was slightly unwieldy and her speech somewhat thick and nasal, but she stated that she had no sore throat, difficulty in swallowing or difficulty in breathing. There were still no symptoms of diminished or excessive activity of the thyroid gland. She had lost about 20 pounds (9 Kg.) in two months, because the foul taste had caused complete loss of appetite. In general appearance she was ruddy, healthy and well proportioned. Her weight was 130 pounds (59 Kg.). The general physical examination revealed nothing unusual aside from the lingual tumor. The pulse rate was 80, the blood pressure 130 systolic and 85 diastolic and the basal metabolic rate +8 per cent. A roentgenogram showed the outline of a mass at the base of the tongue and downward displacement of the epiglottis (fig. 2). The diagnosis was lingual thyroid with central necrosis.



Fig. 1.—Appearance of lingual thyroid with the tongue pulled gently forward (drawing by L. Fletcher).

First Operation (April 7, 1936).—Under local anesthesia the neck was widely explored for thyroid and parathyroid tissue through a transverse incision. At the usual sites there was no glandular tissue, nor was any such found elsewhere, though the dissection was carried well below the sternal notch and above the hyoid bone. Furthermore, examination of both external carotid arteries showed no superior thyroid vessels. Recovery from the operation was prompt and uneventful.

It seemed likely that all the patient's thyroid tissue existed in the lingual tumor. Because of this, operation might have been withheld, but because of the foul odor from the necrosis, which was becoming more and more disagreeable to the patient, and because of the constant danger of hemorrhage from the same source, operation appeared unavoidable.

Second Operation (April 22, 1936).—A tracheotomy was done during local anesthesia through a small incision below the previous exploratory incision. In the next few days the patient learned to tolerate the tracheotomy tube with ease, and the tissues healed nicely.

Third Operation (May 4, 1936).—During anesthesia induced with avertin plus ether administered through the tracheotomy tube, the tumor was approached

through the mouth. The tongue was pulled forward, and soft sea sponges were placed in the pharynx to collect blood and mucus. Double medium silk sutures were placed deeply through the tongue at intervals around the base of the tumor both for traction and for temporary hemostasis. An incision widely encircling the opening of the necrotic sinus was made through the mucosa overlying the tumor. The tumor, which proved to be fairly well encapsulated, was then shelled out of its bed by combined blunt and sharp dissection. As the silk tractive and hemostatic sutures were removed, bleeding from the tumor bed was controlled by transfixion sutures of chromic catgut. Finally, the lappet of mucosa was pulled across the raw surface and sutured in place.



Fig. 2.—Lateral roentgenogram, showing the outline of the mass at the base of the tongue, which partly fills the pharynx and depresses the epiglottis. One of the three radon seeds can still be seen in the substance of the tumor.

Attempted Thyroid Transplant: Immediately after this operation was completed, several thin sections (1.5 by 5 by 5 mm.) were cut from the tumor in a region not involved by necrosis. These were passed through sterile saline solution in the hope of avoiding infection and then implanted in the rectus abdominis muscle. As feared, however, the wound soon showed evidence of infection, and the sloughing tissue extruded itself when the edges of the wound were spread on the fifth postoperative day.

Course: Aside from loss of the transplants, the early postoperative course was not unusual. The patient suffered surprisingly little discomfort from the operation,

and the tracheotomy tube was removed on the seventh day. On the morning of the ninth day bleeding appeared from the wound at the base of the tongue and increased with alarming rapidity. Conservative measures failed, and the patient went into hemorrhagic shock as she was being transported to the operating room two hours after the bleeding had started.

Fourth Operation (May 13, 1936).—With the patient in an extreme Trendelenburg position and with the tongue digitally compressed to retard the bleeding, ether anesthesia was induced with difficulty. (The tracheotomy tube, which, unfortunately, had been removed two days previously, would have served well in this



Fig. 3.—Diagrammatic section, showing the position of the lingual thyroid. Cavitation and a sinus connecting it with the mouth can be seen (drawing by L. Fletcher).

emergency.) The bleeding was largely controlled by a deep suture through the left side of the base of the tongue, but as a further safeguard against a recurrence, an incision was made in the neck and the left lingual artery ligated near its origin from the external carotid artery. The lingual artery was the first branch off the external carotid in this instance, because the superior thyroid artery, ordinarily the first branch, did not exist. After the ligation, bleeding from the tongue stopped completely and the left side blanched temporarily.

Course: After several transfusions of blood, recovery was rapid, and the subsequent course in the hospital was satisfactory. There were no signs of parathyroid deficiency, and the basal metabolic rate before discharge was -7 per cent.

Pathologic Picture.—The tumor measured 5 by 3 by 3 cm. The solid part appeared adenomatous and contained yellowish, necrotic-looking material not very suggestive of the gross picture of thyroid tissue. The cavity of the tumor measured 3 by 1.5 cm. and was filled with foul, sloughing granulation tissue (fig. 3).

Microscopically (fig. 4), the tissue near the cavity showed inflammatory changes, but sections bordering on this area had the appearance of long-standing fetal adenoma of the thyroid. In other words, the thyroid acini were lined with low cuboidal epithelium, frequently empty and widely separated by hyaline connective

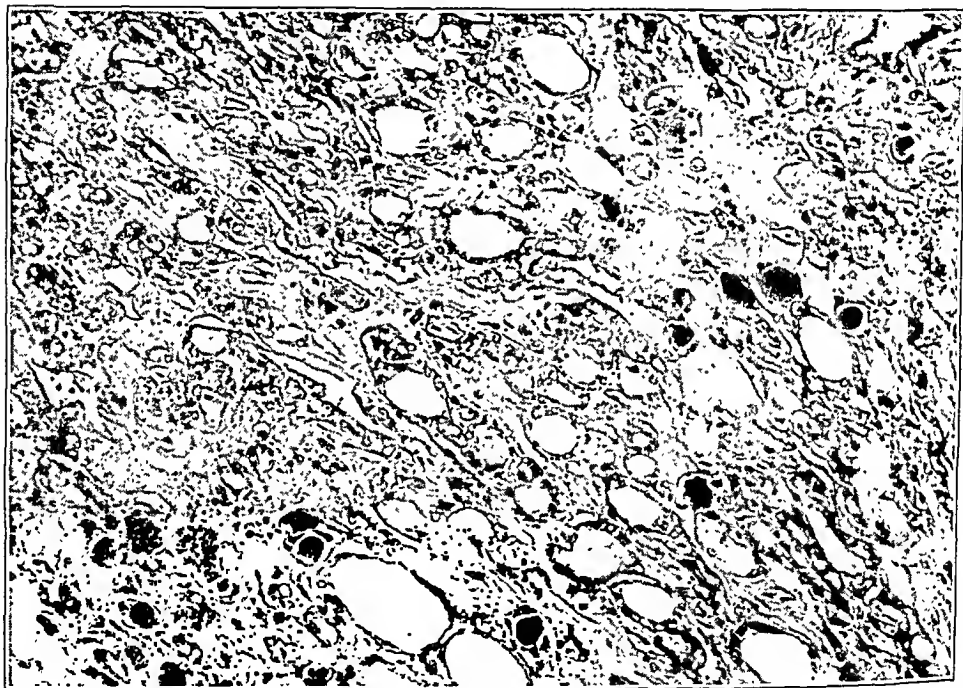


Fig. 4.—Photomicrograph showing fetal pattern of the thyroid.

tive tissue. Possibly one twentieth of the acini contained colloid material, most of which was "immature colloid." Other sections showed numerous cordlike masses of metaplastic cells of thyroid origin. Whether these represented reaction to surrounding inflammation with marked involution or early neoplastic changes was somewhat difficult to decide, but the former hypothesis seemed more tenable. No parathyroid tissue was found.

Follow-Up.—The patient has been observed at regular intervals during the fifteen months since operation. The previously thick speech soon was replaced by clear articulation. Although myxedema had been anticipated, she has steadfastly maintained that her health is excellent and she has no complaints. There has been no listlessness, no complaint of feeling cold, no falling out of hair, no drying of skin and no inordinate gain in weight. Only after eight months was slight

puffiness noticed about the eyes. The following tabulation of the pulse and the basal metabolic rate during the period of observation indicates a gradually increasing hypothyroidism:

		Weight (Kg.)	Pulse Rate	B.M.R. (%)
Before Operation	Feb. 27, 1935.....	65.5	80	—3
	Apr. 2, 1936	55	84	+8
Operation	May 4, 1936			
After Operation	May 25, 1936.....	51	64	—7
	March 23, 1937.....	66	74	—17
	May 24, 1937.....	67	76	—18
	July 24, 1937.....	68	64	—19

A year after operation a small firm nodule about 6 mm. in diameter was noticed far back on the surface of the tongue; this, in all likelihood, was a residual and hypertrophied nodule of thyroid tissue.

Comment.—In this case all the patient's thyroid tissue existed in the gland at the base of the tongue. Its function was adequate, and although it had attained fair size it caused no distress. No doubt it began to grow some time after the age of 28 and might never have been noticed if it had not been found on routine physical examination. Unfortunately, it was thought at first to be a neoplasm and treated as such with roentgen rays and radium. The use of the latter was a mistake, and when it was finally appreciated that the tumor was thyroid tissue, the damage had already been done. With the fetid odor and the danger of hemorrhage from necrosis, there was little choice but to remove the gland. It may be, of course, that, even had the patient been treated conservatively with iodine and thyroid extract, continued enlargement of the gland would have necessitated operation.

The fact that myxedema did not develop within a few weeks after operation can mean only that some thyroid tissue remained attached to the tongue, and this supposition has been substantiated by the appearance of a small nodule in that region. The early signs of myxedema which are appearing after a year, however, indicate that the remaining tissue is inadequate and probably undergoing atrophy of exhaustion.

For first recording a case of lingual thyroid the credit has usually gone to Hickman,² an Englishman, who examined a newborn baby that had suffocated from a large thyroid tumor at the base of the tongue. In an admirable restudy of the literature, Buckman³ unearthed an earlier account by Hunt,⁴ an American, who described what must surely have been lingual thyroid, though it was not entirely recognized as such at the time. The patient was a healthy-appearing girl of 16 and had a tumor arising from the region of the foramen caecum of the tongue and filling the fauces; the tumor had been observed to grow from the size of a pea after the onset of puberty, and its description fit the classic pic-

2. Hickman, W.: Congenital Tumor of the Base of the Tongue Pressing Down the Epiglottis on the Larynx and Causing Death by Suffocation Sixteen Hours After Birth, *Tr. Path. Soc. London* **20**:160, 1869.

3. Buckman, L. T.: Lingual Thyroid, *Laryngoscope* **46**:765, 878 and 936, 1936.

4. Hunt, W.: Tumor of the Posterior Portion of the Tongue, *Am. J. M. Sc.* **51**:163, 1866; *Tr. Coll. Physicians Philadelphia* **4**:153, 1865.

ture now known. To date, about 250 cases have appeared in the literature, and even though in approximately half there have not been histologic studies, other features have been sufficient to allow the diagnosis.

DEVELOPMENTAL ANATOMY

Knowledge of the origin and development of the normal thyroid gland simplifies the understanding of aberrant thyroid tissue. Comparatively early in embryonic life the thyroid arises as an outpouching from the foregut at the level of the first pharyngeal pouches. This diverticulum becomes a sac and is attached to the pharynx by a tubular neck known as the thyroglossal duct. Though the duct eventually atrophies, its point of attachment to the tongue is permanently marked by the dimpled foramen caecum. The thyroid diverticulum is converted into a solid epithelial structure that migrates downward in the neck, where it assumes a transverse position with a lobe on each side of the upper tracheal rings (Arey⁵).

If the thyroid anlage fails to migrate or migrates incompletely, all or a part of the gland may be found anywhere between its point of origin at the foramen caecum and its normal position in the neck. The anomaly under consideration, lingual thyroid, represents persistence of thyroid tissue at its point of origin at the base of the tongue. It is to be differentiated from intralingual or sublingual thyroid, another aberrant form which appears not in the pharynx but in the submental region. In some cases all of the existing gland is present in the lingual tumor. In others the lingual nodule represents only a part of the patient's thyroid tissue, and the rest is to be found elsewhere along the tract of descent. Obviously, the removal of a lingual thyroid will vary in effect, depending on which of these two arrangements exists.

Study of the aberrant thyroid raises the question of the importance of the so-called lateral thyroids. They are known embryologically as the ultimobranchial bodies and arise in the region of the fifth pharyngeal pouches. These bodies detach, migrate caudad and normally fuse with the thyroid gland, but there is no evidence that they become glandular tissue. That they do not is supported by the fact that removal of a lingual thyroid is often followed by myxedema, which should not be the case if functioning thyroid tissue arose from the ultimobranchial bodies.

The parathyroids, which arise from the third and the fourth pharyngeal pouches, likewise fuse with the normal migrating thyroid, but

5. Arey, L. B.: *Developmental Anatomy*, Philadelphia, W. B. Saunders Company, 1931, p. 170.

fortunately they are not fused with the lingual thyroid. Tetany has not been known to follow removal of a lingual thyroid except in 1 case reported by Asch.⁶

INCIDENCE AND ETIOLOGY OF LINGUAL GOITER

Lingual thyroid has occurred in a female subject in 75 per cent of reported cases. It, of course, exists at birth, but its presence is seldom brought to light until later. In a few cases it has been recognized at birth or within the first year, because the size of the tumor was incompatible with life. In a majority of cases the tumor is first noticed during puberty, when its physiologic enlargement occurs. Physiologic enlargement has also been encountered during pregnancy. A striking case (reported by Rubeli⁷) was that of a woman with alarming growth of a lingual thyroid during the last months of pregnancy; a cesarean section was resorted to and was followed by prompt diminution in the size of the gland.

Increase in size of the lingual thyroid has occurred during menopause in 10 per cent of female patients. Beck⁸ reported similar increase following operation for ovarian cysts, and in the case presented here there may have been some relation to the patient's pelvic disorder. Enlargement of a lingual nodule occurred in 1 case after thyroidectomy (Van Selms⁹) and in another after the pathologic destruction of the thyroid gland in the neck (Willis¹⁰). In a few cases this increase has been thought to be associated with trauma and it has been noticed after local and general infection.

GROSS APPEARANCE AND PATHOLOGIC PICTURE

Typically, lingual thyroid occurs as a single centrally placed tumor in the region of the foramen caecum. It is globular or hemispheroidal, with a smooth or lobulated surface, and it is covered by mucosa of the tongue, through which may be seen varying degrees of vascularity. Usually its attachment to the tongue is broad, although in a few cases it has been pedunculated. Bishop¹¹ reported 1 case in which there was such a narrow stalk that removal was simply accomplished with a

6. Asch, R.: Lingual Goiter, with a Contribution to Myxedema and the Question of Postoperative Tetany, *Deutsche Ztschr. f. Chir.* **130**:593, 1914.

7. Rubeli, H.: Lingual Goiter and Pregnancy, *Monatschr. f. Geburtsh. u. Gynäk.* **52**:295, 1920; abstracted, *J. A. M. A.* **77**:78 (July 2) 1921.

8. Beck, J. C.: Surgery of the Tongue, *Ann. Otol., Rhin. & Laryng.* **27**:27, 1918.

9. Van Selms, cited by Buckman.³

10. Willis, R. A.: Compensatory Hyperplasia of Accessory Lingual Thyroid, *J. Coll. Surgeons, Australasia* **3**:257, 1930.

11. Bishop, F. J.: Lingual Thyroid, *Ann. Otol., Rhin. & Laryng.* **43**:294, 1934.

snare. The color varies from light pink to dusky red, depending on the vascularity. The growth is firm and elastic to the examining finger and may vary from an almost invisible nodule to a mass big enough to fill the pharynx and depress the epiglottis (fig. 3). Large lingual thyroids have been described as of the size of a hen's egg or even of an apple, although the usual comparison has been to a walnut. As with other organs, size is no index of function, nor does it give any clue to the presence or absence of thyroid tissue elsewhere. Both large and small lingual thyroids have been found in cretins, and comparatively small ones have been encountered in normal persons who have no other thyroid tissue.

The histologic structure in the majority of instances is like that of normal thyroid tissue, but in about 20 per cent (Montgomery¹²) there is a fetal pattern in which there are areas of solid cell nests and numerous small acini containing little or no colloid. Cystic and other types of degeneration are not uncommon and are to be expected in the large lingual glands in cretins. At least 2 cases in which there were malignant changes are on record (Tyler¹³; Ashurst¹⁴); in both of these the patient was a man. In other cases in which the condition was reported as malignant, the data are not entirely convincing, and it is well to remember that benign fetal adenoma having a poor capsule next to the tongue may closely resemble a rapidly growing and invasive malignant growth.

A similar difficulty has been encountered in determining the presence or absence of parathyroid tissue. Wood¹⁵ reported 2 cases of lingual thyroid in which there were fragments of tissue "resembling parathyroid." In discussion Ewing stated the belief that it was impossible to distinguish between young thyroid tissue and parathyroid tissue. The presence of parathyroid bodies would be difficult to explain from an embryologic standpoint; yet the case reported by Asch seems authentic enough, since tetany developed after removal of a lingual thyroid.

CLINICAL FEATURES

The symptoms may be trivial or even absent, particularly if the lingual thyroid is small and the secretory function adequate. If the growth is large, it is prone to cause difficulty in speaking, breathing

12. Montgomery, M. L.: Lingual Thyroid, *Tr. Am. A. Study Goiter*, 1935, p. 145.

13. Tyler, A. F.: Carcinoma of Lingual Thyroid with Metastasis in Lungs, *J. Radiol.* **4**:381, 1923.

14. Ashurst, A. P. C., and White, C. Y.: Carcinoma in Aberrant Thyroid at Base of Tongue, *J. A. M. A.* **85**:1219 (Oct. 17) 1925.

15. Wood, F. C.: Thyroid and Parathyroid Tumors of the Tongue, *Proc. New York Path. Soc.* **16**:84, 1916.

and swallowing. Other complaints, less frequently mentioned, are pain in the throat, snoring, nonproductive cough, dry mouth, a full feeling in the throat and a constant desire to swallow. In some cases in which the tumor almost fills the pharynx, however, the complaints are minimal. Hemorrhage from the submucosal vessels has occurred in varying degrees in 10 per cent of reported cases. It has usually been the result of local trauma or ulceration, although in several cases it has been concurrent with menstruation.

One should expect, perhaps, that a gland that shows deficiency in development in one respect will show other deficiencies as well. Added to this is the fact that the position of the lingual thyroid allows for limited growth, and the gland is exposed to repeated trauma and inflammation. The incidence of nonfunctioning glandular tissue is comparatively high in cases of lingual thyroid. Frank cretinism or juvenile myxedema has been present in about 10 per cent of reported cases, and in a smaller percentage, adult myxedema has occurred.

Hyperthyroidism might reasonably occur in association with lingual thyroid, but one would expect to encounter it infrequently. Only 2 cases in which there was presumed hyperthyroidism have been reported. In Strauss' ¹⁶ case virtually the same symptoms were present after removal of a lingual gland as before, which throws doubt on the diagnosis. In Perlman's ¹⁷ case there were symptoms of mild hyperthyroidism and a palpable thyroid in the neck as well. After rest and the ingestion of iodine, the patient had no more symptoms, but there was no change in the size of the lingual nodule. The inference is that the hyperplastic thyroid tissue existed in the neck and not in the lingual nodule.

PROGNOSIS OF TREATMENT

It is of considerable importance to know whether the lingual thyroid comprises all or only a part of a patient's existing thyroid tissue. This can be determined often simply by palpation in the normal pretracheal region or in the suprahyoid or the infrahyoid region or most certainly by exploratory operation. The latter procedure, of course, need not be carried out in every case, but there need be little discomfort or danger in it. Montgomery has estimated that in from 65 to 75 per cent of cases there is no other functioning thyroid tissue.

Myxedema will surely follow the removal of a lingual thyroid if no other functioning thyroid tissue exists, and while myxedema can be fairly well controlled, it is not a condition to be induced without good reason. If there is no pressing indication for removal, therefore,

16. Strauss, M.: Thyroid Tumor of the Tongue, *Med. Klin.* **2**:1259, 1906.

17. Perlman, H. B.: Lingual Thyroid Gland, *Arch. Otolaryng.* **19**:594 (May) 1934.

conservative treatment is advisable. Particularly when physiologic hypertrophy occurs during puberty or pregnancy, it would seem wiser to try the effect of iodine and thyroid whenever possible. Even roentgen radiation, carefully used, may be of value, but the case presented here demonstrates the dangers of radium.

The indications for operative removal of a lingual thyroid can be listed as follows: (1) the presence of other functioning thyroid tissue; (2) undue embarrassment in speaking, swallowing or breathing; (3) repeated or dangerous hemorrhage; (4) uncontrollable hyperthyroidism; (5) degeneration with necrosis and (6) suspected malignant changes (the incidence is probably high in male subjects.).

Operation.—When removal is indicated, the method of operative procedure requires careful planning for the individual case. Various lateral approaches have been utilized, but a transbuccal approach appears simpler and more direct. The operation to be described has occasionally been modified to include splitting the tongue longitudinally in the midline, which would appear to be a reasonable variation in case the tumor is unusually large or deeply embedded in the tongue. With a large tumor, the safety and the facility afforded by a preliminary tracheotomy far outweigh the few disagreeable features. It has been the experience of most surgeons that the thyroid is well encapsulated except at its attachment to the tongue, and removal has been comparatively simple. The blood supply to the lingual thyroid comes from the lingual arteries, as demonstrated in this case by the absence of the superior thyroid arteries and by the control of hemorrhage by ligation of the lingual artery.

Subtotal removal has been suggested as a means of preventing myxedema, and it is likely that this has unwittingly been accomplished in some of those cases in which postoperative myxedema has not developed. However, the incidence of recurrence of the lingual tumor in these same cases has been estimated at about 12 per cent. The most reasonable policy is to operate only when there is sufficient indication and then to attempt total removal. If myxedema follows, the patient can be given regular doses of thyroid, and the recent work of Stone, Owings and Gey¹⁸ has given new hope for the use of grafts of thyroid tissue.

18. Stone, H. B.; Owings, J. C., and Gey, G. O.: Living Grafts of Thyroid and Parathyroid Glands. *Surg., Gynec. & Obst.* 60:390, 1935.

RIGHT PARADUODENAL HERNIA

A CASE FAVORING THE THEORY OF TREITZ

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The subject of paraduodenal (internal or mesentericoparietal) hernia is one which has always greatly interested any physician fortunate enough to encounter the condition.

The first report of right paraduodenal hernia was given by Klob in 1861. Nagel in 1923 collected the 29 cases reported up to that time. Exner in 1933 added the 11 authenticated cases reported in the interim, including his own. Novak and Sussman's case was not accepted by Exner, Averbach or us. Since that time 3 further cases have been reported (by Halliwell in 1934, by Bryan in 1935 and by Averbach in 1937), which with the case now being reported bring the total up to 44.

Exner summarized the history of these hernias and segregated them into three periods, as follows:

Period	Cases Reported	Cases in Which Operation Was Done	Cases of Recovery	Correct Preoperative Diagnosis
1861-1903.....	19	4	1	0
1904-1923.....	10	8	1	0
1924-1933.....	11	11	9	2

Since Exner's paper, including this case, 4 cases have been reported; 4 patients have been operated on; 4 patients have recovered and 1 partially correct preoperative diagnosis has been made (Halliwell).

From 1861 to 1923, 29 cases had been reported, with only 2 recoveries. From 1924 to 1937, 15 cases have been reported, in all of which operation was performed and in 13 of which the patients recovered. In addition, during the latter period, 2 correct preoperative diagnoses and 1 that was partially correct have been made.

ETIOLOGY

The cause of paraduodenal hernia has been the subject of wide discussion. The earlier and more generally accepted theory is that of Treitz. Treitz contended that a loop of small intestine insinuates itself into one of the peritoneal fossae at the duodenojejunal juncture and that owing to variations in intra-abdominal pressure the fossa becomes enlarged until a retroperitoneal hernia is formed. In 1923 Andrews suggested that the condition is a congenital anomaly. He stated that it

is due to incarceration during fetal life of the small intestines behind the leaves of the mesentery of the colon. These leaves are thereby prevented from becoming obliterated by fusion against the posterior parietal peritoneal wall.

The case here to be reported lends strong support to the theory of Treitz. In this case the first orifice of the hernial sac was in the usual place for a right paraduodenal hernia, that is, on the left side of the mesentery. A second hernial orifice was found in the lateral parietal peritoneum which extends between the ascending colon and the lateral abdominal wall. The hernial sac had pushed down through the first hernial orifice and had progressed retroperitoneally toward the lateral abdominal wall. It had pushed anteriorly on the parietal peritoneum which runs between the ascending colon and the anterior abdominal wall. The intestines had made and now occupied a large sac. The diameter of the sac greatly exceeded the diameter of the second hernial orifice. The ascending colon was pushed medialward. The sac consisted of two layers of peritoneum.

Any other explanation of the mechanism of formation of this hernia is difficult to understand. The fact that the diameter of the sac exceeded greatly that of the second hernial orifice shows that loops of intestine can form an intra-abdominal sac. Failure to show this has always been the greatest point in favor of Andrew's theory.

ANATOMIC CONSIDERATIONS

In this case of right paraduodenal hernia the opening of the sac was on its left side and faced left. The superior mesenteric artery ran in the neck of the sac anteriorly. Both the afferent and the efferent loop of bowel passed through the hernial orifice.

The literature states that with left paraduodenal hernia the opening of the sac is on the right side and faces left. The inferior mesenteric vein runs in the neck of the sac anteriorly. Exner stated that only the efferent loop of bowel passes through the hernial orifice.

PATHOLOGIC PICTURE

In this case adhesions were present about both hernial orifices. In some cases reported in the literature adhesions were present in the sac as well. Intestinal obstruction was not found at operation in this case, although this was the most frequent finding in the cases reported in the literature. Stenosis and also thickening of the intestinal wall have been reported.

DIAGNOSIS

A correct preoperative diagnosis was not made in this case. Only three such diagnoses have been made, and these were all made roent-

genologically. Apparently the only means by which a correct preoperative diagnosis can be made oftener is the more frequent use of roentgen studies. There were features in this case which should have aroused the suspicion of paraduodenal hernia and warranted roentgen investigation of a barium sulfate meal. The history of attacks of mild, recurrent intestinal obstruction was obtained. While a tympanic abdominal mass was not present, the history alone was sufficient to call for roentgen study.

TREATMENT

In this case the steps in treatment were: (1) Opening of the hernial sac; (2) separation of the adhesions about the two hernial orifices; (3) milking of the intestines back through the two hernial orifices; (4) excision of the hernial sac; (5) closure of the two hernial orifices, and (6) tacking of the ascending colon back into an approximately normal position.

In some cases reported in the literature the adhesions around the neck of the sac have been so great as to make it impossible to reduce the hernia. In such cases it has seemed best to enlarge the neck of the sac downward to release the constriction on the intestines and their blood supply.

In case the blood supply to the bowel were damaged the prognosis would be bad, since most of the small intestine is usually in the sac. Fortunately no such complication was encountered in this case.

REPORT OF CASE

M. M., a white woman aged 21, demanded an appendectomy on March 22, 1937.

She had been well all her life until July 4, 1930. While driving a car at a speed of 38 miles per hour she lost control of the car when it hit some loose gravel. The car rolled over one and a half times, and the steering wheel struck her in the middle part of the abdomen. She had no shock and noticed only moderate abdominal soreness for a day or two.

In October 1936 she had a cramplike, rather severe pain in the lower part of the abdomen, possibly worse on the right side. It lasted three hours. A little tenderness was elicited in the right lower quadrant. A white blood count was not made. She was a little nauseated but did not vomit. She felt some soreness in the lower part of the abdomen for two days. The bowel movements were not irregular after this attack.

In January 1937 she had occasional fleeting pains in the lower part of the abdomen, but these did not interfere with her work as a university student.

On March 2 she had an attack of pain similar to the one which had occurred in October of the preceding year. The pain was probably somewhat more severe. She was a little nauseated but did not vomit. She had a sore throat and a temperature of 105 F.

The history included a tonsillectomy in 1928.

Physical examination revealed a well developed and well nourished woman 70 inches (178 cm.) in height and weighing 155 pounds (70.3 Kg.). The

temperature, the pulse rate and the respiratory rate were normal. The white blood cell count was 8,900. The abdomen was essentially normal.

The preoperative diagnosis was possible mild, recurrent appendicitis. Operation was not encouraged, but was done on March 23 because of the patient's insistence.

A large hernial sac containing about seven eighths of the small intestine occupied most of the right side of the abdominal cavity. The orifice of the sac was on the left side of the mesentery over the lumbar area and measured about 3.5 cm. in diameter. Both the afferent and the efferent loop of bowel passed through it. Along the right, anterior, free edge of the hernial orifice ran the superior mesenteric artery.

The cecum was found slightly to the right of the midline, about 2 cm. below the inferior margin of the hernial orifice. Bands were running between it and the descending colon. At this stage the appendix was removed, which was probably a technical error.

The hernial sac was now opened. No adhesions were found within the sac. Slight adhesions were present about the hernial orifice, but these were separated with moderate ease. When an attempt was made to milk the intestines back through the first hernial orifice, it was discovered that a second hernial orifice was present. This was 3 cm. in diameter and was 3.5 cm. from the inferior margin of the lateral parietal peritoneum which goes to the ascending colon. The adhesions about the second orifice were separated with moderate ease. The hernial sac was ascertained to consist of two peritoneal layers.

The small intestines were reduced back into the abdominal cavity. Both hernial orifices were closed with running sutures of silk reenforced by interrupted silk sutures, the sac of the hernia being excised. The cecum and the ascending colon were separated from the descending colon and were anchored to the lateral parietal peritoneum.

After a somewhat stormy postoperative course complicated by paralytic ileus, the patient recovered. When last seen she was well and function of her bowels was normal.

SUMMARY

The forty-fourth authentic case of right paraduodenal hernia is reported. It is the twenty-seventh case in which operation was performed and the fifteenth in which recovery of the patient occurred.

The findings in this case strongly favor the etiologic theory of Treitz.

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BIBLIOGRAPHY

- Andrews, E.: Duodenal Hernia—A Misnomer, *Surg., Gynec. & Obst.* **37**:740, 1923.
- Arnold, I. A.: Hernia into Paraduodenal Fossa with Large Biliary Calculus: Case, *Kentucky M. J.* **31**:561, 1933.
- Averbach, B. F.: Right Paraduodenal Hernia, *Am. J. Surg.* **35**:128, 1937.
- Barrs, A. C.: Hernia Retroperitoneal, *Lancet* **2**:286, 1891.
- Behr, F.: Der zum Bruchsack ausgeweitete Recessus duodeno-jejunalis (Treitzsche Hernie) im Röntgenbild, *Röntgenpraxis* **3**:744, 1931.
- Bernardbeig: Etranglement de la totalité de l'intestin grêle dans une hernie para-duodénale droite, *Bull. et mém. Soc. nat. de chir.* **51**:284, 1925.
- Broderon, N. H.: Incarcerated Treitz Hernia: Case, *Norsk mag. f. lægevidensk.* **92**:952, 1931.

- Brohec, G.: Les hernies parajéjunales rétroperitonéales ou hernies de Treitz et de Waldeyer, *Arch. d. mal. de l'app. digestif* **21**:794, 1931.
- Brown, F. R.: Right Duodenal Hernia: Case Successfully Operated on; Fourth Recorded Recovery, *Brit. J. Surg.* **13**:367, 1925.
- Bryan, R. C.: Right Paraduodenal Hernia, *Am. J. Surg.* **28**:703, 1935.
- Case, J. T., and Upson, W. O.: Roentgenologic Aspects of Various Types of Hernia, *J. A. M. A.* **87**:891 (Sept. 18) 1926.
- Christophe, L.: Duodéno-jejunosomie pour hernie de Treitz, *Bull. et mém. Soc. nat. de chir.* **52**:1000, 1926.
- Cofer, O. S., and Phillips, H. S.: Duodenal Hernia, *Ann. Surg.* **94**:1088, 1931.
- Copenhagen, N. H.: Intra-Abdominal Hernias, *Arch. Surg.* **7**:332 (Sept.) 1923.
- Crymble, P. T.: Some Factors Influencing the Position of the Small Intestine, *J. Anat. & Physiol.* **49**:216, 1914-1915.
- Deaver, J. B., and Burden, V. G.: Right Paraduodenal Hernia, *S. Clin. North America* **9**:1015, 1929.
- Dott, N. M.: Anomalies of Intestinal Rotation: Their Embryology and Surgical Aspects, *Brit. J. Surg.* **11**:251, 1923.
- Dowdle, E.: Right Paraduodenal Hernia, *Surg., Gynec. & Obst.* **54**:246, 1932.
- Eitel, G. G.: Retroperitoneal Hernia, with Complications, *Journal-Lancet* **46**:131, 1926.
- Exner, F. B.: Roentgen Diagnosis of Right Paraduodenal Hernia: Report of Case with Survey of Literature, *Am. J. Roentgenol.* **29**:585, 1933.
- Fleming, J. A.: A Case of Retro-Peritoneal Hernia, *J. Anat.* **57**:366, 1922-1923.
- Fletchermacher, C.: Hernia retroperitonealis mesenterica mit Einklemmung des gesamten Dünndarmes, Resektion des Bruchsackes, Heilung, *Zentralbl. f. Chir.* **56**:1284, 1929.
- Forlini, E.: Contributo alla conoscenza della cosiddetta fossetta retroperitoneale e delle ernie del Treitz, *Arch. ital. di chir.* **16**:481, 1906.
- Frazer, J. E., and Robbins, R. H.: Factors Concerned in Causing the Rotation of the Intestine in Man, *J. Anat. & Physiol.* **50**:75, 1916.
- Hallivell, A. C.: Right Paraduodenal Hernia, *Brit. J. Surg.* **21**:398, 1934.
- Harris, V. C.: Retroperitoneal Hernia, *Lancet* **2**:240, 1932.
- Hepworth, F.: An Unusual Peritoneal Sac, *J. Anat. & Physiol.* **50**:293, 1916.
- Herbet, H.: Hernie rétroperitonéale duodénale gauche, *Bull. et mém. Soc. anat. de Paris* **78**:889, 1903.
- Jalcowitz, A.: Zur Klinik und Pathogenese der rechtseitigen paraduodénojejunalen Hernien, *Arch. f. klin. Chir.* **160**:449, 1930.
- Le Jeune and Guilloux: Etranglement interne dans un orifice mesenterique, *Bull. et mém. Soc. nat. de chir.* **50**:369, 1924.
- Lower, W. E., and Higgins, C. C.: Retroperitoneal Hernia, *Ann. Surg.* **82**:576, 1925.
- MacCallum, W. G., and Miller, R. T., Jr.: Right Meso-Jejunal Hernia, *Bull. Johns Hopkins Hosp.* **19**:219, 1908.
- Maleolm, R. H.: Two Cases of Hernia into Peritoneal Fossa, *Canad. M. A. J.* **17**:449, 1927.
- Masson, J. C., and McIndoe, A. H.: Right Paraduodenal Hernia and Isolated Hyperplastic Tuberculous Obstruction, *Surg., Gynec. & Obst.* **50**:29, 1930.
- Morton, J. J.: Atresia of the Duodenum and Right Internal Hernia, *Am. J. Dis. Child.* **25**:371 (May) 1923.
- Moynihan, B. G. A.: On Retro-Peritoneal Hernia, New York, William Wood & Company, 1906.

- Nagel, G. W.: Right Paraduodenal Hernia, *J. A. M. A.* **81**:907 (Sept. 15) 1923.
- Novak, E., and Sussman, A. A.: Right Paraduodenal Hernia, *J. A. M. A.* **82**:1664 (May 24) 1924.
- Nuzum, F., and Nuzum, J.: Two Unusual Hernias: One Intersigmoid, the Other into the Paraduodenal Pouch of Landzert, *Tr. Chicago Path. Soc.* **9**:191 and 326, 1914-1915.
- Oberlin, S.: Total Retroperitoneal Hernia of Small Intestine, *Bull. et mém. Soc. nat. de chir.* **58**:1196, 1932.
- Paton, E. P.: Right Duodenal Hernia in an Infant, *Lancet* **1**:971, 1906.
- Philips, R. S.: Paraduodenal Hernia: Description of a Case and Summary of the Literature to Date, *Bull. Ayer Clin. Lab., Pennsylvania Hosp.*, 1922, no. 7, pp. 89-104.
- Primrose, A.: Retroperitoneal Hernia Due to an Aberrant Middle Colic Artery, *J. A. M. A.* **63**:842 (Sept. 15) 1914.
- Rose, E.: Die Eigenthümlichkeiten der Einklemmung bei inneren Hernien, *Deutsche Ztschr. f. Chir.* **40**:513, 1895.
- Scheele, K.: Beitrag zur Diagnostik der Hernia duodenojejunalis, *Zentralbl. f. Chir.* **48**:188, 1920.
- Short, A. R.: Retroperitoneal Hernia, *Brit. J. Surg.* **12**:456, 1925.
- Taylor, J.: The X-Ray Diagnosis of Right Paraduodenal Hernia, *Brit. J. Surg.* **17**:639, 1930.
- Telfer, S. V.: Case of Abnormal Disposition of the Peritoneum, *J. Anat. & Physiol.* **49**:136, 1914-1915.
- Twyman, E. D.: Nonrotated Ileum with Fatal Intestinal Obstruction Due to the Occlusion of the Ileum by the Overriding Colon, *J. A. M. A.* **70**:672, (March 9) 1918.
- Venables, J. F.: Case of Duodenal Retro-Peritoneal Hernia, *Guy's Hosp. Rep.* **80**:313, 1930.

SIXTY-SIXTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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CONGENITAL DEFORMITIES

Klippel-Feil Syndrome.—To the dozen autopsy studies in cases of the Klippel-Feil syndrome Scriba and Gmelin¹ add 1 case in which Sprengel's deformity was also present, as well as a congenital malformation of the heart. The cardiac lesion was the cause of death. The authors point out that anomalies frequently associated with the vertebral synostosis which characterizes the Klippel-Feil syndrome are spina bifida occulta and coordinated malformations such as congenital elevation of the scapula and anomalies of the rib. Associated malformations of the central nervous system, of the gastrointestinal tract or of the heart and the great vessels are seldom seen. In this case both lesions were typical malformations resulting from interference with normal development at some stage. No familial history of either deformity was obtainable, although reports of other cases have demonstrated the existence of a tendency to inheritance of such lesions.

Phocomelus and Absence of the Radius.—Hill² reports in detail the case of a patient with hands and feet but without arms or legs (pho-

This report of progress is obtained from a review of 142 papers selected from 186 titles relating to orthopedic surgery and appearing in the medical literature approximately between Nov. 1, 1937, and March 2, 1938.

1. Scriba, K., and Gmelin, L.: Frankfurt. Ztschr. f. Path. 50:376, 1937.

2. Hill, L. L., Jr.: Surg., Gynec. & Obst. 65:475, 1937.

comelus) and that of another patient with absence of the radius. He was able to find reports of only 3 cases of phocomelus in the literature. Absence of the radius is far more common. Two hundred and fifty-three instances of this deformity were reported up to 1923.

Congenital Dislocation of the Shoulder.—Cozen³ reports in detail the history of a boy aged 4 years with a congenital dislocation of both shoulders. This condition is differentiated from injury to the shoulder at birth by the birth history, by the absence of paralyzed muscles and by the frequent presence of other deformities. In this patient there were cervical ribs, ectrodactylism, radioulnar synostoses and congenital articular rigidity. Reefing of the capsule of both shoulder joints was performed, and later a Nicola operation was required on one side because of redislocation. The boy was examined four years later and was found to have almost normal function in both shoulders. Twenty cases are collected from the literature, attesting the rarity of this condition.

Familial Dissemination of Osteosclerosis.—Busch,⁴ of Copenhagen, Denmark, observed a case of Albers-Shönberg's disease and was able to discover 14 other cases in three generations of the patient's family. One year later a second case was observed, but in the patient's family no other case was discovered after careful search. The disease is distributed about equally between sexes. It is characterized by rounded areas of opacity scattered throughout the skeleton but most numerous about the epiphyses of the long bones. There are areas of whitish yellow infiltration of the skin in about one half of the patients. Pathologic study of the osseous lesions has shown hyperplasia without any inflammatory reaction. The disease is apparently an innocent anomaly of unknown cause, probably the result of faulty embryonal ossification. A review of the literature is given.

Etiology of Congenital Malformation.—Murphy⁵ reviewed 130,132 death certificates of persons dying during five years in Philadelphia. Among these, 1,476 had a congenital defect. Through interviews with the families of the deceased, 45 additional cases of congenital deformity were found. The author was unable to secure any evidence that prenatal environment played a part in producing congenital deformity, as had been suggested by Mall.⁶ However, there was no congenital ampu-

3. Cozen, L.: Congenital Dislocation of the Shoulder and Other Anomalies: Report of a Case and Review of the Literature, Arch. Surg. **35**:956 (Nov.) 1937.

4. Busch, R. F. B.: Acta radiol. **18**:693, 1937.

5. Murphy, D. P.: Am. J. Obst. & Gynec. **34**:890, 1937.

6. Mall, F. P.: J. Morphol. **19**:3, 1908.

tation in this group. Deformity occurred relatively twice as frequently in white persons as in Negroes. The data which the author secured point to heredity as the cause of congenital deformity. The author suggests that reproductive inefficiency was the cause, as shown by relative sterility of the parents before the birth of the deformed child, the presence of deformity in siblings, the frequency of miscarriage and stillbirth among the mothers of such persons and the duplication of defects in brothers and sisters.

[ED. NOTE.—In the two preceding reports of progress papers suggesting a hereditary cause of congenital deformity were reviewed.]

TUBERCULOSIS

Operative and Conservative Treatment of Tuberculosis of the Spine.—The results of treatment in 44 cases of tuberculosis of the spine are discussed by Finkelstein and his associates.⁷ The patients, all under 20 years of age, were divided as nearly as possible into two equal groups. In one group fusion operations were performed on the spine, and in the other group conservative measures alone were employed. A period of ten years is covered. The ineffectiveness of both conservative and surgical treatment is emphasized. The average number of days of hospital care for the patients on whom operation was not performed was one thousand, two hundred and fifteen and for the patients on whom operation was performed eight hundred and seventy-six. The authors conclude that tuberculosis of the spine is a chronic disease which runs its course little influenced by the efforts of the orthopedic surgeon. The discussions form a valuable part of this paper.

Diagnosis, Course and End Results of Tuberculous Spondylitis.—Kofman⁸ analyzes 303 cases of tuberculous spondylitis treated between 1924 and 1932 at the Odessa Tuberculosis Institute. He concludes that surgical treatment of spinal tuberculosis is inadequate. Prolonged immobilization and exposure to sunlight, together with general measures to improve health, have given the most satisfactory results. Operation is indicated only for the relief of spasticity and for the careful aspiration of abscesses. In a second paper the same author⁹ reviews the treatment of adults with spinal tuberculosis in sanatoriums. After conservative therapy the author discharged 147 of 231 patients as improved. Of

7. Finkelstein, H.; Greenberg, B. B.; Jahss, S. A., and Mayer, L.: *Operative and Conservative Treatment of Tuberculosis of the Spine: A Comparative Study*, J. A. M. A. **110**:480 (Feb. 12) 1938.

8. Kofman, S. W.: *Tuberculous Spondylitis*, Committee of Sciences of U. S. S. R., Tashkent, 1937.

9. Kofman, S. W.: Arch. f. orthop. u. Unfall-Chir. **38**:355, 1937.

these, 114 are employed in the lighter forms of work. Sixty-six of the 231 patients died during treatment, 23 within six months of their admission to the sanatorium. Sixty-two per cent of those with closed abscesses and 47 per cent of those with open abscesses showed improvement. The commonest cause of death in patients with draining abscesses was amyloid disease (14 fatalities). Seventy-four patients had visceral tuberculosis in addition to the spinal lesion.

[ED. NOTE.—In any appraisal of end results in the treatment of tuberculosis of the bones and joints the communal standard of health must be considered. The most discouraging reports of the results of therapy come from countries where public health measures are inadequate or from the poorer districts of large cities.]

Osteitis Tuberculosa Multiplex Cystoides.—Connolly,¹⁰ of Liverpool, England, states that multiple cystic changes in bones represent the rarest form of osseous tuberculosis. Such a pathologic change may occur in two ways: (1) there may be caseation followed by fibrous proliferation in bone, or (2) there may be absorption of bone alone. The lesions evolve slowly, and there is a marked tendency to heal. Two cases are reported in detail. In both the patient showed cystic lesions in the phalanges, with scattered lesions in other bones as well.

POLIOMYELITIS

Recovery from Poliomyelitis.—Schein¹¹ has followed carefully all the patients with poliomyelitis treated at the Bellevue Hospital between 1931 and 1936. Over 400 patients were seen, but if those without paralysis and those treated elsewhere are eliminated the number is reduced to 100. More than a fourth of these were in the hospital a year or longer. Fifty-six per cent of patients with paralysis limited to the trunk recovered entirely. Fifty-three per cent of patients with paralysis of an upper extremity showed complete recovery, as against 24 per cent of patients with paralysis of a lower extremity. These figures are similar to those reported by Lovett. Ten patients showed curvature, functional in 6. There was almost complete absence of severe deformity. The deformities least amenable to prevention were flail shoulder, scoliosis and disabilities of the feet. Forty-four operations have been performed on these patients, 19 being stabilizing operations on the feet. Four patients were unable to walk, and of these, 3 have died of pneumonia. Eight patients are using crutches.

10. Connolly, H. E.: *Brit. J. Radiol.* **11**:25, 1938.

11. Schein, A. J.: *New York State J. Med.* **37**:1661, 1937.

Physical Therapy for Infantile Paralysis.—Ober¹² gives a brief, pertinent discussion of the use of physical therapy in the three stages of infantile paralysis. In the first stage, i. e., from the onset of the disease to the disappearance of neural and muscular tenderness, no massage or exercise is given. Absolute rest and daily application of hot packs are insisted on, in addition to the use of whatever splints are necessary to prevent deformities. In the second stage, after all tenderness has disappeared, baking, massage and active exercise are begun. The extent of these is determined by a complete muscular examination, the results of which are recorded on special forms. During the third stage of the disease, i. e., at the end of the period of maximum recovery of power in the muscles, fixed deformities are relieved when possible, and physical therapy is employed during periods of immobilization and rehabilitation. Electricity has no place in the treatment of infantile paralysis.

Rest and Protection in Convalescence from Poliomyelitis.—Bennett and his associates¹³ emphasize that positions of physiologic rest must be constantly maintained while muscles are recovering from poliomyelitis. They described various light splints which are covered with cellulose-acetate compound to increase their wearing qualities and make them waterproof. A much more detailed description of the treatment mentioned by these authors is found in the report of Kendall and Kendall,¹⁴ with a foreword by Drs. Bennett and Johnson, in which are explained and illustrated the methods of protecting weakened muscles during exercise and during rest. A method of grading muscles in percentage of normal function is given.

OSTEOMYELITIS

Acute Hematogenous Osteomyelitis.—Robertson¹⁵ distinguishes between osteomyelitis caused by *Streptococcus* and that caused by *Staphylococcus* by the ability of these bacteria to produce fatal septicemia (13.3 per cent for the former and 22.4 per cent for the latter, in 337 cases). In streptococcic osteomyelitis there is no necrosis of bone, whereas in staphylococcic osteomyelitis there is necrosis. No sequestrums were observed in patients surviving a streptococcic infection, whereas sequestrums were practically always seen in patients with

12. Ober, F. R.: *Physical Therapy in Infantile Paralysis*, J. A. M. A. **110**: 45 (Jan. 1) 1938.

13. Bennett, G. E.; Cobey, M. C., and Kendall, H. O.: *Molded Plaster Shells for Rest and Protection Treatment of Infantile Paralysis*, J. A. M. A. **109**:1120 (Oct. 2) 1937.

14. Kendall, H. O., and Kendall, F. P.: *Care During the Recovery Period in Paralytic Poliomyelitis*, Public Health Bulletin 242, United States Treasury Department, April 1938.

15. Robertson, D. E.: J. Bone & Joint Surg. **20**:35, 1938.

staphylococcic osteomyelitis. Forty-two per cent of the patients under 2 years of age recovered; of these, 80 had sequestrums. A diffusible exotoxin excreted by the staphylococcus has an extraordinarily high potency and the ability to produce necrosis. Three toxins (leukocytolysin, hemolysin and a necrotizing toxin) are combated by the patient's natural antitoxin and phagocytosis. The presence of these toxins may stimulate the production of antitoxin, which can be definitely measured in terms of antihemolytic units. Administration of staphylococcus toxoid can raise the titer of a normal person as much as 16 times, the average normal titer being less than 1 unit. Cutaneous infections, strangely, do not seem to act as efficient antigens in raising the titer. Therefore, Robertson believes not only that children with cutaneous lesions should be protected from injury or strain but that a course of staphylococcus toxoid should be given. Furthermore, the blood of all patients with chronic or healed staphylococcic osteomyelitis should be frequently investigated, and toxoid should be administered if less than 3 units of antitoxin is present. The pathologic picture of experimental and human osteomyelitis is discussed briefly by the author, who gives his observations on the signs and symptoms of the patients he has treated. Regarding treatment, Robertson feels that no help can be had from operation until pus is present, after which simple drainage may be of advantage. In the early stages, treatment consists of combating an infection of the blood and dealing with toxins and organisms present.

Acute Osteomyelitis of the Ilium.—Pique and Valls¹⁶ review in detail the clinical histories of 6 patients with acute osteomyelitis of the ileum, who were treated in the Hospital Durand in Buenos Aires, Argentina. In 5 cases the ilium and in 1 the pubis was involved. The organism responsible was *Staphylococcus aureus* in 5 cases and a streptococcus in 1. The ages of the patients were from 6 to 12 years. The lesions tended to be diffuse and were first observed about osteo-cartilaginous junctions. The most frequent complications were suppurative arthritis involving the sacroiliac joint, the symphysis pubis and the hip joint. The local and general symptoms were similar to those of osteomyelitis elsewhere, but diagnosis was often difficult since the symptoms could simulate those of abdominal or pelvic lesions. The abscesses gravitated along fascial planes and occurred both within and without the pelvis. The commonest deformity was flexion contracture of the hip. There was 1 case of pathologic dislocation of the hip joint. Treatment consisted of local and general measures. The authors favor the use of vaccines. Early operation with wide exposure of the ilium, curettage of the lesion and packing of the wound with petrolatum gauze are advocated. There was 1 death.

16. Pique, J. A., and Valls, J. E.: *Rev. ortop. y traumatol.* 7:1, 1937.

Primary Osteomyelitis in the Adult.—Leclerc¹⁷ finds that primary osteomyelitis in adults runs a somewhat different course from that observed in children. There is often an acute infection years before the occurrence of osteomyelitis. Then there may be an infectious incident, followed by the gradual development of osteomyelitis. The clinical signs are moderate; no great change takes place in the general condition of the patient. In the bone the lesion tends to be localized, with destruction of bone and surrounding eburnation. Incision and curettage are usually followed by healing. Cases are reported to illustrate the course of the disease.

Osteomyelitis in Infancy and Childhood.—Ober¹⁸ states that osteomyelitis is an extremely grave condition in early childhood. There is a difference in the osseous lesions in children under 2 years of age and those in older children. In infants the organism causing the disease is usually the streptococcus. There is rarely a sequestrum. The treatment consists of simple drainage. The limb is immobilized in a plaster cast with a window for dressing, which is performed weekly. Attention to the general condition of the child, particularly to dehydration, delay in operation until the general condition has improved and infrequent application of dressings have reduced the mortality from 50 to 5 per cent. In children over 2 years of age the infecting organism is usually the staphylococcus, and sequestrum formation is the rule. Treatment of these patients also usually consists of simple drainage followed by immobilization. Operation should be performed early if the general condition of the child is good. Sequestrums are often absorbed spontaneously. The various forms of osteomyelitis in children are described briefly.

MUSCULAR DISEASES

Epidemic Myalgia.—Lindberg¹⁹ reviews the previous reports of epidemic myalgia in Sweden and records his own observations of an epidemic of myalgia in the fall of 1938. Eighty children were attacked. In most cases the disease occurred during September. The incidence was greatest at the age of 7 years. Seventy patients were under 12 years of age. Pain appeared without prodrome except slight malaise, usually in the chest or abdomen and occasionally in the neck or arms. The pain was severe. In 25 cases there was swelling of the muscles. In a number of the cases intrathoracic or intra-abdominal lesions were suspected. In most instances there was mild leukopenia; in a few leukocytosis was present, the leukocyte count being 12,000. The sedimentation rate of the blood was followed in 23 cases. A mild increase

17. Leclerc, G.: *Rev. d'orthop.* **25**:227, 1938.

18. Ober, F. R.: *Am. J. Surg.* **39**:318, 1938.

19. Lindberg, C.: *Acta pædiat.* **19**:1, 1937.

in the rate was observed during the course of the disease. Meningitis with increased pressure of the spinal fluid, a positive reaction to the Pandy test and increased cellular content were noticed in 5 cases. All the patients recovered promptly. The duration of symptoms was usually four or five days. No microscopic examination was made of the muscles, nor could the author find record of any pathologic study in the literature. The author believes that the disease is an acute infectious process which spreads much like influenza. The only treatment was symptomatic. All the patients recovered completely.

POSTURE

Teaching of Body Mechanics in Pediatric Practice.—Sweet²⁰ gives an excellent résumé of the problem of body mechanics. He has emphasized the importance of body mechanics as a part of preventive pediatrics. The mechanics of the human body at rest and in motion are reviewed and the fundamentals emphasized under four headings: (1) the part played by gravity; (2) the strength and balance of the muscles; (3) the development of deformities, and (4) body changes during normal growth and development. The teaching of proper posture is discussed, and three points are emphasized: (1) the position of the feet; (2) the rotation of the pelvis, and (3) the position of the head.

Postural Defects Related to Arthritis.—Hartung²¹ states that postural defects can affect patients with arthritis in five ways: 1. Faulty posture is mechanically inefficient and requires an undue amount of energy in standing and sitting, in this way adding an extra burden to the patient. 2. It produces gastrointestinal visceroptosis and decreases the vital capacity of the lung. 3. It predisposes to pain in the lower part of the back. 4. It causes undue strain on certain joints, predisposing them to the localization of arthritis. In osteoarthritis this static trauma localizes the severe expression of the disease to the lumbosacral and the cervical region of the spine and to the knees and feet. 5. It has a depressing psychologic effect on the patient. Since chronic arthritis is a constitutional disease, until a clearer conception of its cause is obtained, the most effective treatment is that directed against the various constitutional derangements presented by the patient. The author's method of correcting faulty posture is described.

THE BACK

Source and Differential Diagnosis of Pain in the Lower Part of the Back.—The problem of location of pain in the lower part of the

20. Sweet, C.: Teaching of Body Mechanics in Pediatric Practice, J. A. M. A. **110**:419 (Feb. 5) 1938.

21. Hartung, C. F.: Arch. Phys. Therapy **18**:626, 1937.

back is approached by Steindler,²² who abandons the old classification into the vertical units of the sacroiliac and lumbosacral and follows instead the routes of the sensory supply to the tissues of the lumbosacral region. First the territories of the posterior and the anterior primary division of the spinal nerves are differentiated, and then the ramifications of the posterior divisions and the structures which they supply are defined. The pathways of the anterior division are dismissed briefly, as they do not involve the immediate problem. Since a large proportion of the cases of pain in the lower part of the back belong to the group in which the trouble involves strictures supplied by the posterior division of the spinal nerves, this type of disorder is discussed in detail. A triad of symptoms, i. e., local tenderness, radiation of pain and faulty posture are recognized, and a series of patients who had localized tenderness and radiation of pain referred to the area of tenderness were chosen. Procaine hydrochloride was then injected into the area. Five postulates had to be met to furnish proof of causal connection between local pain and radiation. The results of the experiments showed that there was such a causal relation and that radiation of pain could be caused by an area of local pain as a reflex symptom without being caused by root compression. This theory does not eliminate true compression of the neural roots caused by special conditions.

[ED. NOTE.—This is a condensed article full of important information; it should be read in its entirety.]

Alternating Scoliosis of Proved Source.—Milliken²³ reports an interesting case of alternating scoliosis in a woman 24 years of age, who had either sciatica on the left and dorsolumbar scoliosis on the right or sciatica on the right and dorsolumbar scoliosis on the left. She complained of pain in the right hip and leg as far as the knee. Roentgenologic examination showed narrowing of the body of the fourth lumbar vertebra with a spur on the upper anterior margin. Operation showed an abnormally long and hook-shaped first sacral spine, which extended upward, meeting a correspondingly long process of the fifth lumbar vertebra. The two processes were not joined but were in contact in the flexed position. Extension of the spine made the processes slip by one another, and a slight twist of the pelvis could make them overlap on one side or the other. Hibbs' fusion of the fourth and fifth lumbar vertebrae and the sacrum was followed by complete relief.

Major Injury to the Spine.—Mixer²⁴ gives an account of the general lines on which treatment should be carried out for severe injury

22. Steindler, A.: Differential Diagnosis of Pain Low in the Back: Allocation of the Source of the Pain by the Procaine Hydrochloride Method, J. A. M. A. **110**:106 (Jan. 8) 1938.

23. Milliken, R. A.: South. M. J. **30**:1099, 1937.

24. Mixer, W. J.: New England J. Med. **217**:899, 1937.

to the spine, beginning at the scene of the accident. For transportation a rigid dorsal stretcher is essential. With injury to the cervical or the upper portion of the spine the patient should be placed on his back; no twisting or flexing of the neck should be allowed. With injury to the dorsal or the lumbar portion of the spine the patient should be placed face downward. As soon as possible the clothing should be cut away and all causes of localized pressure removed. General treatment for shock should be instituted. When the initial shock subsides, a neurologic examination should be made to determine particularly the upper limit of any loss of power or of sensory or reflex abnormality. Roentgen examination should then be made. Time is valuable. If paralysis or neurologic signs persist after two hours, there is probably damage to the cord or the cauda equina, and lumbar puncture to determine the presence or absence of hemorrhage and the presence or absence of block in the subarachnoid space is indicated. If evidence of compression exists, the advisability of laminectomy must be decided. If the pressure is on the spinal cord, it should be relieved as early as possible, i. e., within a matter of hours; if the pressure is on the cauda equina, which is a less vulnerable structure, time is not so important. Cervical fracture with compression is a serious injury. Laminectomy further weakens the spine and causes disturbance of the heat-regulating and the respiratory mechanism. For this reason traction up to 40 or 50 pounds (18 to 22 Kg.) is preferred, and skeletal traction may be necessary. Lumbar puncture is then repeated to determine whether the compression is decreased. If laminectomy then seems indicated, it should be performed within twenty-four hours of the injury. For fracture in the dorsal region with compression and block laminectomy should be performed, since there is little fear of dislocation. The operation should take place within twenty-four hours of the time of injury. For fracture of the lumbar portion of the spine with injury to the cauda equina, laminectomy may be postponed till existing bony deformities are corrected.

Spinal Epidural Cyst with Resulting Kyphosis.—Cloward and Bucy²⁵ give a detailed account of a case of spastic paraplegia in a patient 16 years old. There were dorsal kyphosis and an epidural cyst, which was removed by operation. An account of 9 similar cases from the literature is given, to illustrate the progress of the deformity and the early symptoms. In all except 1 of the cases the patients were adolescent, and all presented alterations in the vertebral bodies at the level of the mass. The commonest site of the lesion was the mid-dorsal region. Kyphosis was present in every case, suggesting kyphosis dorsalis juvenilis. The authors draw attention to the predominance of motor changes and to the fact that in 3 patients no block in the spinal canal

25. Cloward, R. B., and Bucy, P. C.: *Am. J. Roentgenol.* 38:681, 1937.

could be demonstrated by the Queckenstedt test. The most frequent roentgenologic changes were a defect in the anterosuperior or the antero-inferior margin of the vertebral bodies, a reduction of the intervertebral space with prolapse of the nucleus pulposus and wedging of the vertebra. In the spinal canal there may be erosion of the vertebral pedicles or a slight concavity of the posterior surface of the vertebral body. The authors believe that the cyst was an evagination of the arachnoid and the dura mater at the point of emergence of the spinal roots. The kyphosis they consider to be the result of pressure on venous channels between the dura mater and the vertebral body.

[ED. NOTE.—This interesting condition is apparently rare. The patient with kyphosis dorsalis juvenilis usually does not present neurologic disturbances in the lower extremities, nor is the roentgenologic picture similar. In this special type of disease, with epidural cysts, early recognition and operation should prevent the spinal deformity.]

Scoliosis Treated by the Wedging Jacket.—Butte²⁶ analyzes some of the cardinal principles of spinal fusion, with particular reference to the selection of the area to be fused, as applied in the New York Orthopaedic Dispensary and Hospital. Five cases are described, and roentgenograms are presented to illustrate the following points: 1. Every vertebra in the primary curve must be fused unless in an occasional case one of the vertebrae at one or the other end of the curve is omitted to avoid overcorrection of the secondary curve. 2. To be ideal, the area of fusion must include the minimum area of fusion (at least), and its end vertebrae must be parallel to each other and at right angles to the line joining their centers. 3. Actual determination of the area of fusion is not made until correction has been obtained by the wedging jacket. 4. Overcorrection of a curvature is avoided by the "pelvic tilt" examination described by Ferguson. During this the patient sits unassisted, with hands resting on the knees; the pelvis is elevated 3 or 4 inches (7.5 to 10 cm.) on the side of the convexity of the lumbar curve, and a roentgenogram is made. 5. Provided compensation has been restored, remarkable improvement in clinical and roentgenographic appearance often results when the primary curve has been corrected less than 50 per cent.

PERIPHERAL VASCULAR DISEASE

Treatment of Peripheral Vascular Disease.—Holman and Schulte²⁷ apply a suction-pressure chamber only to the thigh, where it acts as a "booster pump," drawing blood into the thigh and forcing blood into the peripheral vessels. In this way vessels which are still patent and pliable instead of obliterated or practically obliterated vessels are acted on.

26. Butte, F. L.: J. Bone & Joint Surg. 20:1, 1938.

27. Holman, E., and Schulte, T. L.: Surgery 2:502, 1937.

The pump can be applied in the presence of infection of the foot, without danger of spreading infection by active massage, and it is useful in cases of obliterative vascular disease, whether the condition is due to thromboangiitis or to arteriosclerosis.

Popliteal Aneurysm as a Cause of Peripheral Circulatory Disease.—Theis²⁸ reports 5 cases of aneurysm of the popliteal artery in which the primary symptoms were those of peripheral circulatory disease. He concluded that an aneurysm in the popliteal space should be suspected in all cases of peripheral circulatory disease. All 5 patients were men. Violent muscular effort was the probable etiologic factor in 2 cases; in the others the cause was not known. Theis believes indirect trauma, such as that resulting from forced flexion of the knee or violent muscular strain, to be the most important cause of popliteal aneurysm.

THE KNEE

Injury of the Knee Joint.—Dickson²⁹ gives an excellent discussion of injuries to the semilunar cartilages, the internal lateral ligaments and the cruciate ligaments. Most of the discussion concerns the semilunar cartilages and presents in detail and in clear textbook form the present day conception of the causes, symptoms, diagnosis and treatment of injuries to these structures.

THE SHOULDER

Rupture of the Supraspinatus Tendon.—Davies and Sullivan³⁰ report 5 cases of complete rupture of the supraspinatus tendon in which the patient was seen within seventeen days after injury. One patient was operated on five days after injury, 2 six days after, 1 thirteen days after and 1 seventy days after. All were in the sixth decade of life. The immediate trauma causing this condition was a fall in 3 cases, a blow in 1 and strain in lifting in 1. Pain was a variable symptom. The authors advise immediate repair, as the operation is easier and the end results better than when it is delayed. Immobilization in 90 degrees of abduction for three weeks after operation is the most satisfactory after-treatment.

Tears of the Supraspinatus Tendon.—Outland and Shepherd³¹ give a résumé of 12 cases of operation for tear of the supraspinatus tendon. One patient was 32 years of age, but the average age for the series was 50 years. The authors stress five objective signs in making the

28. Theis, F. V.: *Surgery* 2:327, 1937.

29. Dickson, F. D.: *Injuries of the Knee Joint*, J. A. M. A. 110:122 (Jan. 8) 1938.

30. Davies, T. W., and Sullivan, J. E.: *Ann. Surg.* 106:1059, 1937.

31. Outland, T. A., and Shepherd, W. F.: *Ann. Surg.* 107:116, 1938.

diagnosis: (1) diminution or loss of power to abduct; (2) tenderness over the greater tuberosity; (3) undue prominence of the greater tuberosity; (4) crepitus, and (5) normal roentgenographic appearance. In 5 of their cases the rupture was the result of dislocation of the shoulder. Hence, they advise testing all patients with dislocated shoulders immediately after reduction. For two thirds of the patients the end results were excellent or good.

[ED. NOTE.—These two papers describe a not uncommon injury which sometimes follows insignificant trauma to elderly persons. In the sixty-fifth report of progress, in a report of a paper by Meyer, the frequent observation of this injury in the dissecting room is mentioned.]

NEOPLASMS

Solitary Bone Cyst and Giant Cell Tumor.—Discussing 6 of his 12 cases of cyst and giant cell tumor, Szanto³² contrasts the views of European and American pathologists. He comments on the necessity of evaluating each case purely on its detailed merits. He agrees that the prognosis for giant cell tumor and solitary cyst occurring in a patient over the age of 24 often is not as benign as in the young. He also agrees that lesions on the diaphysial side of the epiphysial plate are more prone to be benign, while the prognosis of those extending on both sides of the plate site, as in older patients, is apt to be less favorable. He disagrees, however, with the American teaching that insufficient surgical intervention may change the character of the lesion and maintains that other causes must be found for progress of the lesion when progress occurs.

Cavernous Hemangioma of the Vertebral Column.—Hemangioma of bone, including that of the vertebral column, is not rare according to Yuzhelevskiy.³³ It is often not recognized clinically. The author was able to find only 34 recorded cases of hemangioma of the vertebral body which caused compression on the spinal cord. He adds reports of 3 cases in which myelitis resulted from vertebral hemangioma. The lesion was in the first lumbar, the fifth thoracic and the eleventh thoracic vertebra respectively in these 3 cases. In 2 the condition was diagnosed at operation, while diagnosis was made from the course and the roentgenologic findings before operation in 1 case. The roentgenograms show bone of cellular and spongy texture with numerous clear spaces divided by fairly thick trabeculae containing calcium. The intervertebral disks were not involved. All 3 patients recovered after operation. When the tumor cannot be completely removed because of its position, laminectomy with postoperative roentgen or radium therapy is of benefit.

32. Szanto, G.: Arch. f. orthop. u. Unfall-Chir. **38**:336, 1937.

33. Yuzhelevskiy, A. S.: Vestnik khir. **52**:164, 1937.

MISCELLANEOUS STUDIES¹

Os Centrale Manus, an Accessory Bone in the Hand.—In both wrists of a 14 year old girl Schneider³⁴ observed at autopsy a cartilaginous accessory bone, os centrale manus. This bone was boat shaped and measured 10 by 7 cm. Such a bone is uncommon, and its ossification takes place later than does that of the other carpal bones. It lay proximal to the dorsoventral canal of the carpal bones. This canal, which contains fat and ligaments, shows occasionally in roentgenograms as an indentation in the neck of the os capitatum. On one side an os capitatum secundarium was present also.

Histiogenesis of Paget's Disease.—Continuing the studies on Paget's disease begun by Erdheim and Freund, Karplus³⁵ studied the development of a lesion in a long bone. He points out that the lesion appears in small multiple discrete areas in the cancellous bone and cortex, which later fuse. He lists several stages. 1. In the immediate neighborhood of an adult spicule of bone a capillary enlarges; round cells appear, and the endosteum over the bone thickens. 2. Osteoclasts are visible in Howship's lacuna eroded into the old bone. 3. The lacuna is deep and is partially or completely filled with new-formed bone. The fatty marrow is replaced by fibrous marrow. These stages are observable not only in the medullary cavity but in the cortex. When the latter area is affected the capillary in the vascular canal of the haversian system undergoes the changes previously listed. Incidentally, the architecture of the new-formed bone appears to bear a relation to the stresses involved. Photomicrographs illustrate the author's explanation of these changes.

Osteochondritis of the Hip Joint.—Since October 1936 4 cases of osteochondritis dissecans of the hip were observed by Schörcher³⁶ in a Munich clinic. All the patients were males. In 2 the disease was bilateral. The ages ranged from 18 to 49. The duration of pain was two months for 1 patient. For the 3 other patients it was six, fifteen and 19 years, respectively. All showed the roentgenologic picture of osteochondritis dissecans. One had some acetabular changes. There was no definite history of trauma. In 1 patient a loose body was found in the hip joint. The author was unable to state what influence injury might have in the development of the lesion.

Method of Treating Ganglions.—Aspiration of the tendon sheath rather than operative removal is advocated by Bearse.³⁷ The aspiration

34. Schneider, H.: Wien. klin. Wchnschr. **50**:1326, 1937.

35. Karplus, H.: Frankfurt. Ztschr. f. Path. **50**:190, 1937.

36. Schörcher: Arch. f. orthop. u. Unfall-Chir. **38**:362, 1937.

37. Bearse, C.: Ganglions of Tendon Sheaths: Method of Treatment, J. A. M. A. **109**:1626 (Nov. 13) 1937.

is performed with a large bore transfusion needle, since the ordinary aspirating needle is not large enough to evacuate the gelatinous contents through its base. Aspiration is followed by tight bandaging for twenty-four hours. In some of the reported cases the condition recurred, but was cured by another aspiration. In 1 case seven different ganglions have been successfully aspirated after two operations for previously appearing ganglions.

ORTHOPEDIC OPERATIONS

Tendinoplastic Amputation Through the Femur at the Knee.—Callander³⁸ gives the essentials of his previously described operation for amputation of the lower end of the femur. The operation begins with creation of an anterior flap running down as far as the tibial tubercle and of a longer posterior flap. The muscles are divided through their tendinous portions, and hemorrhage is thereby lessened. The popliteal vessels and nerves are ligated through a medial approach to the popliteal space. The patella is removed, its tendon being left intact, and the femur is divided just proximal to the adductor tubercle. After the end of the bone is treated, the flaps are held together with widely spaced skin sutures. None of the deep structures are sutured. The redundant skin is rapidly drawn taut by postoperative contraction of the hamstring muscles, and the scar is converted by this pull into a posterior one. The author has recorded 80 cases of amputation by this method. Most of the patients were elderly persons (over 65 years of age). The operation was performed chiefly for vascular complications. The operative mortality was 13 per cent.

New Suture for Tendons and Fascial Repair.—Gratz³⁹ describes a method of suturing divided tendons whereby the strength of the internal fixation is increased. Reinforcing figure of eight sutures are placed and tied in a V behind the tendons. This allows firm, accurate apposition without danger of pulling out of the retaining sutures.

FRACTURES

The Most Resistant Fracture.—Hoffman,⁴⁰ of Geneva, Switzerland, reviews the methods of treatment for fracture of the femoral neck, giving credit to Delbet for the introduction of a screw or nail for internal fixation by a small incision over the trochanter. In discussing the problem of nutrition of the femoral head he quotes the law of Roux, of Lausanne, Switzerland: "Upon the skeletal structures, all pressure produces bone, all traction produces fibrous tissue." He believes this

38. Callander, C. L.: *Tendoplastic Amputation Through the Femur at the Knee: Further Studies*, J. A. M. A. **110**:113 (Jan. 8) 1937.

39. Gratz, C. H.: *Surg., Gynec. & Obst.* **65**:700, 1937.

40. Hoffman, R.: *Rev. d'orthop.* **25**:193, 1938.

law is of fundamental importance in the prognosis of fracture of the femoral neck. With recent fracture one may wait as long as ten days and correct any organic defect before considering operation. If the position is favorable for function and pressure will be exerted on the fracture by muscular pull and weight bearing, it should be maintained. In cases in which the position of the fragments is not so favorable the patient should be operated on if there are no contraindications. With the patient under spinal anesthesia, the legs are put in traction with gradual bilateral abduction. This brings the femoral neck into valgus. Over a Kirschner wire as a guide and under roentgenologic control a pin is driven into the femoral head. A pillow under the knee is the only support after operation. Active motion in bed is encouraged in one week. Early walking is permitted only in cases in which the line of fracture is horizontal. In other cases unprotected walking should be delayed four months. Pseudarthrosis is caused by failure of contact under pressure of the fractured ends. Usually in cases of nonunion simple osteotomy is performed subtrochanterically. Then an attempt is made to bring the surface of the fracture to a horizontal position.

Fracture of the Femoral Diaphysis.—Bado and his co-workers⁴¹ review 85 cases of fracture of the diaphysis of the femur treated at the Hospital Pasteur in Montevideo, Uruguay. Skeletal traction was employed, usually through the femoral condyles. When full reduction was secured and easily maintained, a plaster spica carefully modeled to the leg was applied from the rib line to the toes. Walking in the cast was begun in six or seven weeks by adults. There were 20 transtrochanteric fractures, 57 in the shaft and 8 above the condyle. Traction was usually continued for from ten to twenty-two days. No operative reductions were performed in this series of cases.

The Discus Articularis in Colles' Fracture.—Taylor and Parsons⁴² point out the importance of recognizing injury to the discus articularis at the distal end of the radius and ulna in Colles' fracture. The function of the discus articularis is to stabilize the inferior radioulnar joint. In Colles' fracture with a loss of integrity of the radioulnar joint the deformity may be due to: (1) rupture of the ligament itself; (2) avulsion of the ulnar styloid at its base, or (3) severe comminution of the lower end of the radius with the ligament attached to a loose minor medial fragment. Diagnosis is made not only by loss of integrity of the wrist but by bulging forward of the ulnar head on the ulnar aspect of the wrist and its abnormal movability in relation to the radius and the hand; also, there is marked broadening of the joint, roentgenographic evidence

41. Baldo, J. L.; Rolfi, D. V., and Pedemonte, P. V.: *Rev. ortop. y traumatol.* 7:91, 1937.

42. Taylor, L. W., and Parsons, C. L.: *J. Bone & Joint Surg.* 20:149, 1938.

of fracture through the base of the ulnar styloid or separation of the medial fragment of the radius. Treatment consists of prompt, accurate restoration of anatomic relations, under fluoroscopic guidance. Impaction should be broken up, and restoration of the dorsal position of the ulna should be accomplished. After the proper length and articular angle of the radius have been restored, there should be close apposition of the radius and the ulna to prevent widening of the wrist. The most stable position is extreme flexion and ulnar deviation (so-called Cotton-Loder position), which should be maintained for ten days in plaster of paris. Then the wrist should be placed in a neutral position for ten days. Disability usually lasts two months.

Isolated Fracture of the Triangular Bone.—Garraud,⁴³ of Lille, France, lists this fracture as rare. Fracture of the triangular bone, associated with other injuries of the hand or wrist, is seen a little more frequently. A case is reported in detail. The injury occurred in a fall on the ulnar side of the extended hand. The diagnosis can be made only by roentgenograms taken with the hand in half supination and in neutral position as regards flexion of the wrist. The fractures may occur by two mechanisms: (1) a pull through the dorsal radiotriangular ligament when the hand is in hyperflexion and radial deviation, or (2) the compression of the bone between the triangular fibrocartilage and the pisiform bone. The fracture heals readily, and rigid immobilization is unnecessary. Support with a splint during the period of swelling is all that is required. The author was able to find only 50 cases of such fracture recorded in the literature.

Fracture of a Metacarpal Bone.—Jahss⁴⁴ flexes the metacarpophalangeal joint to the involved finger 90 degrees and reduces the displacement by upward pressure. This method is used for any of the four fingers. The position relaxes the interosseous muscles and tenses the collateral ligaments. The proximal fragment is then immobilized in plaster of paris, which is allowed to dry, after which a second plaster of paris strip is applied around the flexed finger to exert a push upward to hold the reduction. The uninvolved fingers are left free.

Injury to the Upper Tibial Epiphysis in Sport.—Holldack⁴⁵ describes the occurrence of an epiphysial separation at the upper end of the tibia of a 16 year old boy during a high jump. There was a loud noise and pain while the boy was in the act of jumping. He was unable to arise from the sand pit. Roentgenograms revealed that the upper epiphysis of the tibia was separated, tilted backward and displaced slightly medially. No other pathologic condition of bone was demonstrable.

43. Garraud, R.: Rev. d'orthop. 25:205, 1938.

44. Jahss, S. A.: J. Bone & Joint Surg. 20:178, 1938.

45. Holldack, F.: Arch. f. orthop. u. Unfall-Chir. 38:379, 1937.

Reduction was followed by uncomplicated convalescence. The lesion was apparently caused by muscular pull and is similar to the avulsion of the tibial tubercle in sprinters. The author was unable to find record of a similar case.

Fracture of the Os Calcis.—Yoerg⁴⁶ treats all types of fracture of the os calcis except that of the beak and simple fracture of the tuberosity by manual manipulation, with complete mobilization of the subastragalar joint. With the achilles tendon relaxed, the heel is pulled down and the disimpacted fractured bone replaced, a clamp being used. A cast is then applied; it is molded under the malleoli, over the back of the heel and under the arch of the foot, with the knee flexed and the foot in full plantar flexion. The cast is removed after one month; removal is followed by massage and active motion without weight bearing for the next four to six weeks. In the ordinary type of fracture union is complete two months after reduction.

Pathologic Fracture.—Ghormley and his associates⁴⁷ review 660 cases of pathologic fracture from the records of the Mayo Clinic and divide them into three groups. The first group consisted of fractures attributable to metastatic malignant lesions. Carcinoma of the breast was the most frequent lesion in this group, causing six times as many fractures as the next known cause, carcinoma of the prostate. The second group contained factors attributable to primary malignant lesions of the bone, the most frequent of which was osteogenic sarcoma followed by myeloma. The third group consisted of fractures caused by benign lesions, of which senile osteoporosis caused three times as many as the next disease on the list, osteitis fibrosa. The various diseases in which pathologic fracture may occur are discussed. The percentages of patients suffering from the various conditions who might be expected to have pathologic fractures are tabulated.

RESEARCH

Fractures and Vitamin C.—Lauber and his co-workers⁴⁸ produced fractures of the forelegs of rabbits in two ways: (1) by fracture of both bones subcutaneously, and (2) by open operation, a 2 mm. segment being excised from the radius. They found that on the second day there was a decrease in the output of vitamin C, indicating the need for more vitamin C. Increasing the intake of the vitamin did not hasten the healing of the fracture; however, giving less vitamin C

46. Yoerg, O. W.: *Surgery* 2:493, 1937.

47. Ghormley, R. K.; Sutherland, C. G., and Pollock, G. A.: *Pathologic Fractures*, J. A. M. A. 109:2111 (Dec. 25) 1937.

48. Lauber, H. J.; Nafziger, H., and Bersin, T.: *Klin. Wchnschr.* 16:1313, 1937.

retarded healing. They conclude that if there is a lack of vitamin C, callus formation may be speeded up by administration of the vitamin. Callus formation was not increased by giving ascorbic acid above the normal vitamin C intake.

Calcium Tolerance Curves in Cases of Paget's Disease.—After studying the calcium tolerance curves of a series of 146 persons, including 17 patients with untreated Paget's disease and 22 normal subjects, London and Bernheim⁴⁹ conclude that in the presence of this condition there appears to be an increased affinity for calcium on the part of the bones and tissues or a decreased affinity for calcium on the part of the blood. They injected 10 cc. of calcium gluconate intravenously, withdrew samples of blood fifteen minutes and two hours later and made determinations on the serum. The curve of patients with untreated Paget's disease showed a tendency to smaller deviations than that for normal controls and that for patients with miscellaneous conditions. Five patients with Paget's disease had an almost flat curve, a result not obtained for any of the normal subjects.

Production of Osteosarcoma in the Mouse.—Brunschwig and Bissell⁵⁰ believe they have reported the first osteosarcoma experimentally produced by a clinical agent. A mixture of 1,2 benzpyrene and cholesterol injected into the intramedullary space of the mouse's tibia produced osteosarcoma in eight and one-half months.

Osseous Changes in the Fetus Produced by Calcium and Viosterol.—Fifty-eight women were placed under observation at various periods of gestation for the remainder of their pregnancy.⁵¹ Thirty-three of them were treated with dicalcium phosphate and viosterol, while 25 served as controls. It was found that the total calcium content of the serum in the treated group increased slightly during the later part of pregnancy, while in the control group there was a definite diminution. The values for the total calcium and for inorganic phosphorus of the infants exceeded those of the mothers, and this difference was more pronounced in the treated group. There was definite evidence of increased density of bone in the majority of infants born to the treated mothers. The authors suggest that this osteosclerosis, especially in the parietal region, might possibly interfere with molding of the head, which is so often an important factor in cases of difficult delivery.

49. London, I. M., and Bernheim, A. R.: J. Lab. & Clin. Med. 23:18, 1937.

50. Brunschwig, A., and Bissell, A. D.: Production of Osteosarcoma in the Mouse by Intramedullary Injection of 1, 2-Benzpyrene, Arch. Surg. 36:53 (Jan.) 1938.

51. Finola, G. C.; Trump, R. A., and Grimson, M.: Am. J. Obst. & Gynec. 34:955, 1937.

Replacement of the Semilunar Cartilage.—Bruce and Walmsley⁵² observed a partial regeneration of the internal semilunar cartilage of a football player who later injured the external semilunar cartilage in the same knee. The replacement was apparently of firm fibrous tissue. In 5 of 6 dogs from which the external semilunar cartilage was removed a similar regeneration with fibrous tissue was seen. This was an ingrowth from the articular capsule and not a growth from the remaining portion of the semilunar cartilage. The authors suggest that a more even substitution occurs when the cartilage is removed completely.

52. Bruce, J., and Walmsley, R.: Brit. J. Surg. **25**:17, 1937.

CORRECTION

In the article by Drs. Curry and Taylor, entitled "Fractures of Both Bones of the Leg," which appeared in the May issue (ARCH. SURG. **36**:858, 1938), the roentgenogram which appeared as figure 3 should have been figure 6, and that shown as figure 6 should have been figure 3.

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FANTOM LIMB PAIN

A REPORT OF TEN CASES IN WHICH IT WAS TREATED BY
INJECTIONS OF PROCAINE HYDROCHLORIDE NEAR
THE THORACIC SYMPATHETIC GANGLIONS

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After the amputation of an extremity it is usual for the patient to have sensations that are ascribed to the absent limb. In the majority of cases these sensations are most vivid immediately after the amputation and as time passes tend gradually to fade from consciousness. Not infrequently, however, the absent limb becomes the apparent site of such severe symptoms that the patient not only becomes more keenly aware of the phantom limb than of his normal extremities but may be so distracted by the unbearable quality of his pain that he loses his social usefulness.

The attention of the surgeon who undertakes to relieve pain in the phantom limb is naturally concentrated on the nerves in the stump, not only because they are the conveyors of painful sensation but because they represent the only type of tissue at the site of amputation that continues to grow. The skin, the muscle, the fascia and the bone tend toward atrophy rather than toward continued growth, but the individual nerve fibers continue their blind effort to grow down into the absent limb. Meeting with resistance, they snarl up into a twisted mass, which if large enough to be palpated is called a neuroma. Various methods of treatment of the cut ends of nerves have been advocated to prevent the formation of neuromas, but it is probable that some degree of piling up of nerve fibers in the scar tissue takes place at the cut ends of all nerves, no matter what method of treatment is used. Such a neuroma may or may not become hypersensitive. A definite neuroma which on palpation causes a shocklike sensation flashing out into the phantom limb over a known nerve distribution can sometimes be treated successfully by local excision and injection of alcohol into the cut end of the nerve.

But pain in the phantom limb, described in the case histories which follow, is decidedly different from the pain caused by a hypersensitive neuroma. The condition may exist in the absence of palpable neuromas. The stump may seem faultlessly constructed. Usually the stump is

cold; sometimes it is clammy with sweat, and occasionally it is discolored and edematous. None of these characteristics, however, appears to be essential to the condition, since the pain may occur in the absence of any of these objective findings. Perhaps the local coldness of the stump is the most constant objective finding, although I have observed 1 case (case 8) in which the attacks of pain were associated with actual increase in the temperature of the stump and dilatation of the veins. In most cases there are vasomotor and sudomotor disturbances in the stump. The most constant and annoying symptom of which the patient complains is a sensation of "tension." One sufferer gave a most impressive illustration of this sensation. He asked me to clench my fingers tightly over my thumb, strongly flex my wrist and then raise my arm behind my back in the "hammer-lock" position. I was told to hold this posture. At the end of three minutes the discomfort in my hand and arm had grown unbearable, and I was perspiring freely. I took my arm down and relaxed my stiffened fingers. "Yes," he remarked, "but *you* can take your arm down."

As Leriche¹ has pointed out, the pain seems to be out of all proportion to any objective findings in the stump, so that to the observer it may appear to be grossly exaggerated. The bizarre symptoms ascribed to an extremity that is no longer present, the inexplicable variations in their intensity and the fact that the subject may be diverted at times so as temporarily to forget his pain all suggest that the pain is "central" and hence not amenable to surgical treatment. Such a conclusion seems to be borne out by the concomitant signs of nervousness, excessive sweating, exaggerated reflexes and emotional instability that frequently are associated with the syndrome of fantom limb pain.

In this paper I shall not enter into a discussion of this explanation of the pain picture, except to concede that a protracted period of suffering from any cause will profoundly affect a patient's ability to tolerate pain. In such a state of hypersensitiveness the patient may interpret as painful a number of afferent impulses which ordinarily are below the pain threshold. But my observations of patients with pain in the fantom limb do not allow me to escape the conviction that there is a physical basis for the original pain phenomena. Just what that physical basis may be is still obscure, but that it exists I cannot doubt. In my capacity as medical examiner for the state industrial accident commission of Oregon I have had the opportunity to examine a considerable number of men who have had amputations of an upper extremity. The proportion of these who feel pain in the fantom limb is surprisingly high, and the similarity in their complaints is so striking as to warrant the term "fantom limb pain *syndrome*."

1. Leriche, R.: Les douleurs des moignons d'amputation, *Presse méd.* 40: 869-873, 1932.

Ten cases have been selected for report in this paper. In all of these the patients have had one or more injections of procaine hydrochloride near the thoracic sympathetic ganglions of the affected side. In 8 of the cases the patient felt immediate relief from pain, together with an extraordinary sequence of subjective and objective changes. In 4 of these 8 cases the relief was of sufficient degree and duration to suggest that injection of procaine hydrochloride is of therapeutic value in such cases. However, the purpose of this paper is not to advocate any particular method of treatment but rather to call attention to the pain syndrome by the presentation of actual cases and to discuss briefly the implications of the observations here recorded in relation to the general problem of pain.

REPORT OF CASES

CASE 1.—C. W., a man aged 54, lost his right hand on July 15, 1929. His hand was jerked into a sprocket wheel, from which it could not be extricated for several minutes. A few hours later the mangled hand and forearm were amputated about 2 inches (5 cm.) below the elbow. He did not suffer any unexpected amount of pain during the month required for the healing of the surgical wound. When he left the hospital, at the end of six weeks, he was conscious of a "deep, heavy pain" in the top of the right shoulder. In the next few weeks this pain became gradually eased, but in the same interval he became increasingly aware of the absent hand. It felt as if it were in a cupped position, tipped slightly toward the ulnar side. He was not able to move any of the fingers. At times he would feel "cramps" in a finger or in the whole hand associated with a "smarting, tingling sensation." When the stump was exposed to cool air the forearm would feel "icy cold." This sensation rarely involved the phantom hand, which was more commonly the seat of a burning sense of heat, "as if it were held too close to a hot stove." He complained of "shooting pains" in various parts of the hand, but his chief complaint was of a sense of "terrible" tension, "as if the muscles were set and the skin too tight." When this sensation was most intense the sweat would pour from the axilla so as to soak his shirt and sleeve. In times of emotional excitement he could be diverted so as to forget his pain momentarily, but there was a peculiarly unbearable quality in it that prevented him from reading or doing any sedentary task. Although the pain was described as being worse during the day, his sleep was fitful and he stated that he was "worn out" with pain.

The stump was well constructed and of normal color. It was cold to palpation and extremely hyperesthetic. He seemed to tolerate light touch less well than a firm grasp of the stump. At each end of a curved scar across the cubital fossa was a definitely localized point of special tenderness which had been called a neuroma. Similar neuromas had been excised previously from other areas, without relieving the pain. When these sensitive spots were touched the patient would jerk away and complain of a shocklike pain which required several minutes to subside. He constantly guarded the stump with his other hand and was of the impression that this guarding continued even during his sleep. Motion at the shoulder and elbow was restricted, and the muscles were weak. When one flexed the elbow sharply there was precipitated a clonic jerking of the stump which he could not control. There was a tendency for the jerking to come on spontaneously. He was seen to rub the stump gently with his other hand at times. He explained

that rubbing the stump seemed to alter the character of the pain in some fashion, but he was not sure that it was diminished materially by the action.

When a sphygmomanometer cuff on the upper part of the arm was inflated just sufficiently to cut off the arterial circulation, he reported a definite relief from the pain. One could then touch the "neuromas" without eliciting the shock-like pain. In addition, he reported that the feeling of tension in the phantom hand was distinctly less. When the pressure was released the stump flushed normally, and the sensitiveness returned within a few seconds.

On Jan. 14, 1931, 8 cc. of a 1 per cent solution of procaine hydrochloride was injected in the region of the stellate and the second dorsal sympathetic ganglion on the right side. Horner's syndrome (slight) was noted, and the temperature of the stump rose several degrees. With the rise in temperature he reported a subjective sense of warmth and relaxation in the absent limb, which he said was most pleasant. He felt that he could move his fingers one after the other. The neuromas in the stump could no longer be located by the patient. He could flex his elbow without precipitating the clonic jerking. The phantom hand felt comfortable and relaxed for several hours after the injection. There was some return of the feeling of tension the next morning, but during the two succeeding days, in which he remained under observation in the hospital, the discomfort, tension and jerking, as well as the local hyperesthesia of the stump, were much less than before the injection. On the basis of the degree of temporary relief afforded by the procaine hydrochloride I advised a sympathectomy, but because of the uncertainty of the final results the operation was not authorized. At that time I had no reason for thinking that the temporary benefit might persist, and my attention was focused on the interesting observation of the disappearance of the neuromas during the test. I have been unable to trace this patient and cannot state whether or not his pain recurred in its original severity.

CASE 2.—X, a physician aged 41, sustained a puncture wound of his left hand in 1926, when a glass syringe containing *Bacillus welchii* broke as he was injecting the bacillus into a guinea pig. Virulent and rapidly spreading gas gangrene made its appearance in the arm during the night, and on the following morning the arm was amputated about 2 inches (5 cm.) below the shoulder. For several days the wound bubbled gas and drained quantities of serous material. He felt pain in the phantom hand from the first day after the amputation. There was a sensation that came and went in the thenar eminence as if a sharp scalpel were being repeatedly driven into the flesh. The fingers seemed to be tightly clenched over the thumb, and he could not relax them. At times the whole arm felt as if it were held in rigid extension. After exposure to cold the tension increased, particularly in the thumb and in the first two fingers. When the sensation reached a certain intensity he felt a "boring" pain that began in the tip of the index finger, ascended the hand to the wrist and then spread in a diffuse manner over the entire phantom limb. The pain required about thirty seconds to reach the shoulder, at which time the muscles of the shoulder girdle began a series of rapid jerking contractions which he was unable to control. When the pain was at its height he became pale and was nauseated. As the pain faded, the sense of tension in the fingers was diminished, but never to a degree sufficient to permit them to be moved. In the intervals between the sharper attacks of pain he felt a persistent "burning" in the hand. The pain was not unbearable, and at times he could be diverted so as to forget it for a short interval. When it became annoying a hot towel thrown over the shoulder or a drink of whisky gave him partial relief.

On June 28, 1932, during a particularly severe bout of pain, an injection of procaine hydrochloride solution was given near the cervicothoracic sympathetic ganglions on the left side. Horner's syndrome was present. He reported that the individual fingers of the phantom hand began to feel warm and to relax, and for the first time in years he felt that he could move the fingers. He could not precipitate pain by moving the stump, slapping it or doing any of the maneuvers that had previously brought on an attack. When the effect of the procaine hydrochloride wore off the pain did not recur to the degree in which it had been present before the injection, and he enjoyed a considerable amount of relief for six months.

More than a year after the first injection this patient returned, complaining of severe pain which he said was of a different type from that which had been felt previously. He had never had a recurrence of the "boring" pain, and the clonic contractions of the stump no longer bothered him. For several months, however, he had been aware of increasing tension in the phantom hand and an intolerable feeling of constriction around the shoulder girdle. He had been on a hunting trip in Canada about a month before I saw him. The weather had been chilly, and although he wore a woolen sock over the stump it had become cold. He believed that the exposure had aggravated his distress. The stump was extremely cold, having a temperature 10 or 12 degrees (F.) lower than that of the trunk. His shirt was constantly wet with perspiration for its whole length on the side of the amputation. On Oct. 12, 1934, 5 cc. of a 2 per cent solution of procaine hydrochloride was injected near each of the upper four thoracic sympathetic ganglions on the left side. When the second needle was inserted below the second rib he complained of a sharp, stabbing pain in the base of the thumb. This phantom thumb was felt to be tightly compressed within the palm by the clenched fingers. An hour after the injection all of the digits except the thumb felt warm and relaxed. The thumb remained pressed into the palm, and a few hours later he noticed an intense sense of burning in this digit, which soon spread to involve the hand and arm. The pain lasted all night, so that he slept less than two hours in spite of the use of a hypnotic. The next day the burning sensation gradually disappeared, and that night he slept soundly for nine hours. In the three years that have elapsed since this second injection there has never been a return of his original pain. The stump has remained warm and less sensitive, there is no jerking of the muscles, and he considers himself "cured."

CASE 3.—R. H. D., a man aged 54, lost his right hand on Oct. 31, 1933. He was employed in a shingle mill and became caught in a saw which severed the right forearm in its middle third and slashed a great wound in his chest and abdomen. At the end of nine weeks his wounds were completely healed, but there was restriction in the range of motion at the shoulder. He also began to complain of pain and sensitiveness in the stump and of increasing tension in the phantom hand. The arm and shoulder muscles began a convulsive jerking which was annoying and uncontrollable. This was associated with "cramping" in the fingers. He said it felt as if there were a wire down the center of his arm to which his fingers were attached. He also spoke of feeling as though some force were pulling on the wire "as if to pull the fingers up through the arm." At times the hand felt hot, as if held by force too close to a hot stove, and the fingers became the seat of intolerable burning. He could not move the fingers voluntarily, out they tended to shift their position over one another, and in so doing would "get caught in cramps." The thumb was apt to abduct and then slowly draw down over the fingers with great force; then the wrist would slowly flex strongly, and the whole hand and wrist would ache. Interspersed between the muscular

contractions he felt knifelike stabs of pain through the hand and fingers. When the burning sensation was absent the general feeling of the hand and wrist was one of coldness, although this was seldom of an unpleasant degree.

As the patient's symptoms progressed he was noted to have a rapid pulse, to tremble all over and to sweat profusely while talking to the examiner. His physical and mental attitude showed a shrinking away from all contacts, and he was incapable of carrying out the simplest transactions. He could not read for any length of time, and his sleep was disturbed. Hyperesthesia of the stump prevented him from wearing his artificial limb. The jerking of his muscles, his mental attitude and what was considered an exaggerated hyperesthesia of the stump led to his being classed as a patient with "hysteria." He repeatedly refused to consider a closure of his claim against the state industrial accident commission, claiming that his pain prevented him from ever doing any work again. A long course of physical therapy, excision of numerous "neuromas," correction of dental sepsis and psychotherapy failed to bring about the slightest improvement in his condition.

In June 1935 a 2 per cent solution of procaine hydrochloride was injected near the third, fourth and fifth thoracic sympathetic ganglions on the affected side. A small amount of iodized poppyseed oil was injected through each needle before it was withdrawn, and subsequent roentgenograms showed the material deposited along the sides of the vertebral bodies near the ribs from the third to the sixth. There was no Horner syndrome, but there was a prompt subjective sense of warmth and relaxation in the fingers of the fantom hand. The thumb slowly moved outward from the fist position, and one by one the fingers opened. The stabbing pains and the jerking of the stump ceased. The two neuromas which had been marked out on the stump before the injection were no longer sensitive.

Examined in November, the patient was found to be wearing his artificial limb continuously. He said he occasionally felt sensations of cold or transient pains in the fantom hand and that at rare intervals the shoulder muscles would jerk, but he expressed himself as delighted with the improvement in his condition. The hyperesthesia of the stump was gone; he slept soundly at night; he had gained in weight, and the change in his physical and mental attitude was apparent in his demeanor and in his request for closure of his claim.

CASE 4.—R. A. H., a man aged 45, lost his left arm in a railroad accident on April 26, 1934. While working as a brakeman he fell with his elbow across the rail; a train wheel passed over the upper part of the arm and the forearm. He sustained multiple fractures of the ribs, shattering of the pelvis, rupture of a kidney and dislocation of a hip. The partial amputation was completed in the hospital within five hours of his accident. He remembered little of what went on around him for the first four weeks. In June he began to notice an increasingly painful tension in the fantom hand, which soon obscured all his other discomforts. The hand felt as if it were tightly clenched, and in cold weather it would ache as if it had been struck a hard blow. When the pain was severe he could not rest. He could always tell when he was about to fall asleep because the fingers would seem to relax slightly, and the hand would drop forward at the wrist. Later, the forearm became painful, "as if it had been scratched and skinned from the elbow to the wrist." The fantom hand seemed smaller than the remaining hand, and the arm seemed short. The arm felt as it were in a position of elbow flexion, but he thought that if it were hung straight down it would reach about to his waist. The stump was so hyperesthetic that he could not permit its being washed; it had become foully dirty and was covered with flakes of dead skin. He could not lie in any position which put strain on the involved shoulder. A patch of skin in

the cubital fossa was said to itch severely. He was unable to move his fingers from the fist position. At times the fingers would press harder into the palms, the nails would feel as if they were pressed inward "toward the bones," the wrist would flex and the pain would become "dreadful." During the three months before he was given an injection of procaine hydrochloride he slept only under the influence of hypnotics, and the fitful sleep did not rest him. He trembled and perspired freely. He cried when attempting to carry on a conversation, and he talked frequently of suicide.

In September 1935 procaine hydrochloride was injected near the thoracic sympathetic ganglions on the left side from the second to the fifth. Severe pain promptly developed in the precordial region. He became extremely pale; his respirations were shallow, and his pulse was rapid and weak. Although this alarming reaction lasted but a few minutes, he continued to complain of pain in the left side of the chest for about three weeks. This pain occupied his attention, but he reported a sense of warmth and relaxation in the phantom arm. He felt that he could move all the fingers except the index finger.

This man was examined at frequent intervals in the year and a half following the injection. His multiple injuries combined to produce permanent total disability. His syndrome of phantom limb pain, however, remained alleviated. The stump stayed warm and dry and lost its hyperesthesia, so that it could be kept clean and soft. There was no longer need to guard the shoulder. He said that he would gladly submit to another injection and accept the risk of another complication in the chest similar to that following the previous injection, but no further injections have been required.

CASE 5.—C. H., a man aged 60, had his right arm partially avulsed at the shoulder when it became caught in a gear in November 1931. The amputation was completed within a few hours, and a large denuded area in the axilla was partially covered with grafts of skin from the abdomen. He was not particularly conscious of the phantom hand during the first six weeks after the amputation. He then began to have three different types of pain ascribed to the absent limb. The first sensation was a continuous burning heat, "like fire in the fingers and hand." The index finger was least affected; the thumb and remaining three fingers were most affected. The second sensation was that of "tightness" associated with a sense of "trembling, drawing and twisting" in the hand and arm. The third type of pain was intermittent and was described as "shooting stabs of pain" throughout the limb. These pains were variable in intensity, but he claimed never to have been free from them for more than twenty minutes during his waking hours. He did not think that his sleep was seriously disturbed and stated that the arm "goes off to sleep two or three times before I can get to sleep." He wore a steel-reinforced leather shield over the shoulder to protect it from any contact, the scar being so sensitive that blowing one's breath across it caused him to cringe and the shoulder muscles to jerk.

At the time of the injection in October 1935 the phantom hand was described as being in a clawlike position, which he could not alter except by moving the index finger slightly. This patient knew that some sort of test was to be performed on his back, but I had purposely refrained from explaining the procedure or telling him what he might expect from it. Procaine hydrochloride was injected near the thoracic sympathetic ganglions from the third to the sixth, and he was asked to report any changes in sensation. He promptly reported that the hand was becoming warm and that he could move all of his fingers. There

was a pleasant sense of relaxation, and the "twisting" tension disappeared. The scar was no longer hyperesthetic, and the jerking of the muscles subsided. In the next few days the phantom hand, which had always felt somewhat smaller than normal, seemed to shrink still more, so that the arm felt to be about 6 inches (15 cm.) long and the hand "about as big as a dollar." Examined three months after the injection, he reported a satisfactory degree of relief, but fourteen months later he returned, complaining of a recurrence of the original pain. On the day he was brought to me by his local physician he had a sharp stab of pain, so severe that he fell to the floor in a faint. On Dec. 14, 1936, a 2 per cent solution of procaine hydrochloride was injected near the third to the seventh thoracic sympathetic ganglion and was followed by the injection of a small amount of dilute solution of quinine and ethyl carbamate (urethane). He again reported a prompt relief from pain and tension, but by March 1937 the fingers no longer felt movable, although the pain had not recurred. The dorsum of the hand was said to feel colder than the palm. In May he reported that the pain had come back. A thoracic ganglionectomy was performed by the posterior approach, the fourth and fifth sympathetic ganglions being excised and the proximal end of the chain being buried in intercostal muscle. Again there was relief from the pain, but within a month it had begun to come back. In August I injected procaine hydrochloride near the stellate ganglion, without appreciably altering his subjective complaints, and later in the same month I divided the brachial plexus high in his neck. The nerve trunks were divided close to the vertebral foramina, alcohol was injected, and the cut ends were closed with fine silk sutures. I regret that I cannot say definitely whether or not the division of the nerve trunks was proximal or distal to the point at which the gray rami join them. The nerve trunks at the point of section were not involved in scar tissue and appeared normal in cross section. Instead of relieving his pain, the operation made it worse. He said that the hand was as tense as ever and the pain unbearable. He entered the hospital in December 1937 prepared for a chordotomy, but he wished me to try more injections of procaine hydrochloride first. An infiltration of the first, second and third thoracic ganglions with 2 per cent solution of procaine hydrochloride relaxed and warmed the hand. The pain was again completely relieved, but at this writing an insufficient interval has elapsed to permit decision as to whether or not repeated injections will help him permanently.

CASE 6.—J. C., a man aged 40, had his left hand severed at the wrist by a wood saw in September 1931. Infection developed in the stump, and multiple incisions were made in the forearm. Healing was complete in two months, during which interval he felt considerable pain in the stump but was not particularly aware of the phantom hand. With the clearing of the local infection, however, his pain seemed to center in the hand. It felt as if it were in a rigid cupped position. He complained of severe burning, most intense in the index finger and thumb. At times the index finger seemed to begin jerking and the whole arm gradually became involved in an uncontrollable twitching. He complained of an ache in the shoulder which spread down the arm to the hand, after which sharp stabbing pains occurred in the fingers. In the interval between September 1931 and July 1935 he had four operations on the stump, three for neuromas and one for the excision of scar tissue and a small exostosis on the end of the radius. None of these operations gave him relief. The stump was cold and clammy, and there were slight edema and cyanosis at its end. The skin could be moved freely over the bones, but subjectively this part of the skin felt as if it were drawn over the ends of the bones like tight parchment.

In July 1935 procaine hydrochloride solution was injected near the second to the seventh thoracic sympathetic ganglion. There followed a prompt relief from pain and tension in the phantom hand and in the stump. He felt that he could move the fingers for the first time since the accident, and, although the hand had not felt particularly cold previously, it was now agreeably warm. Examined in January 1936, he stated that the fingers had gone back to their cupped position. He could no longer move them but stated that the tension was not great. He had not obtained complete relief from pain in the phantom hand but said that the remaining pains were bearable. The stump no longer felt tight, and he could tolerate wearing his artificial arm, which he had been previously unable to wear. He had secured a job and wished to continue with it, promising to return for further injections should they be needed.

CASE 7.—G. M., a man aged 43, in October 1934 had his left hand and forearm caught in some gears, which "chewed up" the tissues so completely that amputation just below the elbow was necessary. He complained of occasional cramping in his fingers, which seemed to be maintained in a tightly clenched posture, but his chief complaints related to the stump. It was cold much of the time but at times would become flushed and hot, sometimes showing "welts." It was usually of a cyanotic color. He had had neuromas removed three times, and the stump had been remodeled twice. In May 1935 the ulnar nerve had been resected 3 inches (7.5 cm.) above the elbow, and alcohol had been injected into its proximal end. These operations had afforded little, if any, relief. In January 1936 procaine hydrochloride was injected near the second to the sixth thoracic sympathetic ganglion. Beyond a slight warming of the stump there were neither subjective nor objective evidences of improvement. He was then given a long series of treatments by alternating pressure in a pavaex unit, which afforded more temporary relief than any treatment previously given.

On December 7 and 8 he was given injections of procaine hydrochloride solution. The first injection was in the region extending from the level of the third to that of the seventh thoracic ganglion, and the one on the following day was in the region of the first to the fourth ganglion. No appreciable benefit was conferred by either injection. In the latter part of the same month his arm was reamputated through the middle third of the upper part of the arm, and an effort was made to conserve for skin flaps only areas of skin that had been least cold and discolored. He noticed immediate relief after this operation. Examined in November 1937, the stump was again cold and cyanotic. It was becoming increasingly hyperesthetic, and he was aware of a feeling of increasing tension in the phantom hand. He insisted that his condition was still better than it had been before the reamputation, but there was evidence suggesting that his original symptoms were returning.

CASE 8 (courtesy of Dr. Howard Naffziger).—L. A. P., a man aged 51, "wrenched" his left shoulder in climbing a trestle in September 1930. A month later he began to notice numbness and tingling in the fingers, and the hand gradually assumed a cadaveric appearance. In November the index finger and the distal joint of the thumb were amputated for spreading gangrene. The wounds failed to heal. Conservative treatment was unavailing, and in January the hand was amputated above the wrist. The stump healed by primary intention within ten days, but the agonizing pain that had been present before the amputation recurred within two days of the operation and remained constant. In March 1932 a "sympathectomy" was done, but the report does not make clear exactly what procedure was carried out, and when I examined the patient in February 1936 there was no evidence of a vasomotor change in the stump, and Horner's

syndrome was not present. In May 1932 a periarterial sympathectomy was done on the brachial artery, and in September of the same year a muscle was divided in the cervical region. None of these operations conferred any lasting benefit.

The patient complained of recurrent series of sharp pains in the fantom hand. It seemed to be tightly clenched, and he was unable to open it. The pains were aggravated when he felt nervous and were partly relieved by bromides. They were definitely worse when the stump was warm, and for the preceding three years he had been subject to periodic attacks in which the veins of the forearm would become distended and the stump more red and hot than usual. At such times the pains were invariably worse. There was no extreme hyperesthesia of the stump, but he was unable to tolerate for long the wearing of an artificial limb. The peripheral arteries were no longer palpable. No increase in sweating had been observed.

In February 1936 solution of procaine hydrochloride was injected near the upper thoracic sympathetic ganglions, without producing appreciable subjective or objective changes.

CASE 9.—A. A. P., a man aged 52, had his left arm crushed between his automobile and a street car in February 1933. When he recovered consciousness after the accident his arm had already been amputated close to the shoulder. He complained of "terrific" pain in the fantom limb present "from the very first minute." In addition to a constant and intolerable feeling of tension, the fingers felt as if the flesh were being torn from around the nails. The wrist felt as if a tourniquet or a wire were tightly constricting it. The arm seemed to be flexed at the elbow, with the forearm extended from the body and the fingers in a cupped position. At intervals this posture changed involuntarily to the extended position of the elbow, and then the fingers would clench tightly into the palm. Although he could not alter the position voluntarily, the hand would occasionally "get to going," the fingers would slide over one another and twist and the hand would "jerk." The jerking would always extend to involve the stump, and he was in the habit of grasping it tightly to prevent its "flapping about." Even when the stump was tightly held the jerking of the muscles would persist. The hand felt "constantly cold and damp," "as if it were in cold water." The pain in the hand was aggravated by taking cold food or drink and also by cold weather. In June a dorsal sympathectomy was performed. The patient was left with a Horner syndrome, but there was no relief from pain and the sweating persisted. He stated that the left side of his body sweat more than the right and that this involved the entire side rather than only the axillary region. In the fall of 1933 an operation on the brachial plexus failed to give him any relief. He had become dependent on large doses of dilaudid hydrochloride supplemented by phenobarbital sodium and sodium amytal for the relief of pain and to permit him to sleep. At the time I examined him, in August 1936, he was using more than a grain of dilaudid hydrochloride daily.

The stump was soft and warm. There were a few sensitive spots in it, but no definite neuromas and no excessive hyperesthesia. When one stroked downward along the stump he complained that it caused an unbearable pressure to be transmitted into the hand. On Aug. 24, 1936, procaine hydrochloride was injected in the region extending from the level of the third to that of the seventh thoracic ganglion. There was an immediate subjective sense of relaxation in the hand, but no feeling of warmth was present. In the ensuing week he described a variety of new experiences and sensations in the fantom limb, all of them interpreted by

him as indicative of improvement. There was no jerking of the muscles, and the stump was slightly warmer to palpation. The arm had changed to the extended position, but the fingers were not clenched. Downward stroking of the stump did not cause discomfort.

On October 1 the injection was repeated, since he still complained of pain in the hand. This time he reported a definite subjective warming of the hand, increased freedom of motion at the shoulder and still more reduction in the pain. He said that his left upper eyelid felt "less heavy" and he thought that it drooped less. I was unable, however, to confirm this impression. A few weeks later he said that he was greatly relieved of pain and was rapidly ridding himself of his dependence on opiates. However, subsequent indirect reports indicated that he continued his addiction and, after an automobile accident in which he was shown to be at fault, had been committed to a state hospital. I have not been able to secure an accurate report of his condition as regards pain in the phantom arm.

CASE 10.—E. C. P., a man aged 50, crushed his hand and forearm in some carding rolls in October 1934. The crushed tissues became infected, and after three months of draining, during which time the patient complained of terrible pain in the hand and fingers, an amputation was done just below the elbow. The operation did not relieve the pain, and for a time he insisted that the fingers were still on. He complained of pain under the finger nails, across the knuckles and in the palm of the hand. There was a constant ache in these parts, which was aggravated when he smoked cigarets, "as if the fingers swelled more." The stump was sensitive to both deep and superficial contact, and the skin covering it felt extremely "tight." He suffered from sudden shocklike pains which came on "like the kick of a mule" at irregular intervals of the day or night, sometimes as often as twenty-four times in one day. The phantom hand was described as being in pronation, with the fingers fixed in a clawlike position and the thumb extended. He believed that he could move his wrist slightly but said he could not move his fingers. He made attempts to clench the hand into a fist, feeling that movement of the fingers might ease the pain. At odd times the stump might jerk suddenly, but he had no clonic contractions and no twitching of the muscles. The stump was well constructed, and the tissues were soft. The skin was of normal color but was colder than normal. I was unable to get a blood pressure reading from the upper part of the arm. When the cuff pressure was maintained above 120 mm. of mercury (the systolic pressure for the normal arm) he reported a feeling of relaxation in the hand and in the stump. The stump might then be palpated without causing him distress. No definite neuromas were found.

In January 1936 solution of procaine hydrochloride was injected near the third to the eighth thoracic sympathetic ganglion on the left side. He became pale, and his blood pressure dropped so that it could not be recorded. He was nauseated and wet with perspiration. The heart action was slow and the sounds distant for more than an hour. For several days after the injection he complained of pain in the left side of the chest "around the heart." During the same interval he felt a distinct warming and relaxation of the phantom hand. The stump was warm and had lost its hyperesthesia. There was a definite increase in the range of motion at the shoulder. The relief afforded by the injection remained satisfactory for about three months. His wife then wrote me that the pain seemed to be coming back, but up to the present time (January 1938) he has not returned for further injections.

COMMENT

On reviewing the literature I find that the method of treating fantom limb pain by infiltration of the sympathetic ganglions with procaine hydrochloride is not new. In an article dealing with repeated injections in the region of the stellate ganglion for a variety of painful conditions, Leriche and Fontaine² stated that patients with neuralgia in the amputation stump have been relieved of pain by this method. In the brief paragraph given this subject they made two interesting observations: first, that the method has proved so successful as a means of treatment that they have abandoned all surgical operations on such patients; second, that they have found it of distinct advantage also to inject the solution near the second thoracic ganglion. In fact, they concluded that better results can be obtained by giving the injection in the region of the second thoracic ganglion alone than by injecting the solution near the stellate ganglion.

Until recently most surgeons in treating vasomotor syndromes affecting the upper extremity directed their attack on the stellate ganglion. This ganglion was selected as the focal point because in it were supposed to lie the postganglionic cells of the vasomotor nerves to the arm and hand. Presumably, all impulses originating in the preganglionic cells in the midthoracic portion of the spinal cord must pass through this ganglion to reach the brachial plexus. My own early operations on the sympathetic pathways of the upper limb were directed at the stellate ganglion, but in June 1931^{3a} I operated on a patient in whom dense adhesions between the pleura and the vertebral bodies in the region of the stellate ganglion blocked my dissection and led to the removal of the third thoracic ganglion only. The immediate result was so satisfactory that in the following month^{3b} I deliberately confined my operation to the third thoracic ganglion.³ Since that time I have come to believe that a sympathectomy at the level of the third thoracic ganglion gives results superior to those obtained by an excision of the stellate ganglion. Not only does the operation at a lower level prevent the appearance of Horner's syndrome and leave intact important pathways from the spinal cord to the head and the thoracic viscera, but the end results seem to be better in that there is a more nearly complete relief of symptoms and recurrences are fewer. Smithwick⁴ and Telford,⁵ independently, have come to the same conclusion.

2. Leriche, R., and Fontaine, R.: *L'anesthésie isolée du ganglion, étoilé*, Presse méd. **42**:849-850, 1934.

3. Livingston, W. K.: *The Clinical Aspects of Visceral Neurology*, Springfield, Ill., Charles C. Thomas, Publisher, 1935, (a) p. 145; (b) p. 101.

4. Smithwick, R. H.: Modified Dorsal Sympathectomy for Vascular Spasm (Raynaud's Disease) of the Upper Extremity, *Ann. Surg.* **104**:339-350, 1936.

5. Telford, E. D.: Technique of Sympathectomy, *Brit. J. Surg.* **23**:448-450, 1935.

Different explanations have been offered as to why the operation at a lower level gives better results. Kuntz⁶ called attention to the relatively constant bundle of fibers connecting the second thoracic ganglion with the brachial plexus and suggested that sympathetic fibers from still lower levels may ascend in the vertebral canal to join the lower nerves of the brachial plexus by way of the corresponding intervertebral foramina. In view of this contribution it appears that functioning sympathetic fiber tracts may be left intact when the operation or injection is confined to the region of the stellate and the second thoracic ganglion. White⁷ and Smithwick⁴ considered the operation on the stellate ganglion to be essentially a "postganglionectomy" and the operation at a lower level to be a "preganglionic section," and they interpreted the better results following the latter operation as due to the fact that after postganglionic fibers degenerate the blood vessels become hypersensitive to the action of circulating epinephrine and the sensitivity following preganglionic section is considerably less. Personally, I have come to feel that the hypersensitization to epinephrine observed in experimental animals after postganglionic section has been overemphasized in attempts to explain the unsatisfactory results of cervicothoracic sympathectomy in the treatment of human beings with vasomotor disturbances. It has never been proved that there is not in the third thoracic ganglion (or even lower) in human beings an important component of postganglionic cells related to the upper extremity. I have felt that some such possibility as this may account for the better results obtained by operations below the second thoracic level as compared with the results of those centering in the region of the stellate ganglion. At least, in my experience, injections of procaine hydrochloride in the region extending from the second to the level of the sixth or seventh thoracic ganglion by a technic modified from the method of Labat⁸ have given more complete and lasting results than injections in the region of the stellate ganglion.

In some of the cases of phantom limb pain here reported, the beneficial effects of the injection have persisted for weeks or months. These are not isolated observations confined to cases of phantom limb pain. Flothow⁹ and White⁷ have reported cases of painful syndromes in which a single diagnostic injection of procaine hydrochloride afforded

6. Kuntz, A.: *The Autonomic Nervous System*, J. A. M. A. **106**:345-350 (Feb. 1) 1936; *The Autonomic Nervous System*, Philadelphia, Lea & Febiger, 1929.

7. White, J. C.: *The Autonomic Nervous System*, New York, The Macmillan Company, 1935.

8. Labat, G.: *Regional Anesthesia*, Philadelphia, W. B. Saunders Company, 1930.

9. Flothow, P. G.: *Injections of the Sympathetic Nervous System*, California & West. Med. **44**:182-186, 1936.

lasting relief. This persistent benefit is difficult to explain because under ordinary circumstances after local infiltration or regional blocking of a peripheral nerve the anesthetic action disappears within a few hours. One may assume that the injection of the drug directly into the ganglions destroys some of the nerve cells, as it is well known that the toxic action of procaine hydrochloride is greater when it acts on nerve cells than when it acts on nerve fibers. This assumption seems to be supported by the observation that persistence of the increase in surface temperature of the stump and a lasting reduction in the amount of sweating may accompany the relief of pain. However, it is not necessary to make such an assumption, because procaine hydrochloride acting only on nerve fibers may also result in a lasting relief of pain. Infiltration with procaine hydrochloride around painful joints, into muscle, around major blood vessels or in sensitive scars often is followed by an interval of complete cessation of pain long after the anesthetic effect has disappeared. If the pain recurs, the next injection may bring about a still longer interval of relief, and repeated injections may afford a "cure." This is true particularly in the obscure types of pain associated with phenomena indicating that the sympathetic nerves are overactive. For the past few years I have been using this method of treatment, with a considerable degree of success, in cases in which long-continued, atypical pain in the extremities followed traumatic lesions. It is difficult to see why the relief from pain should persist in some cases and not in others, but I am inclined to think that the procaine hydrochloride temporarily interrupts a vicious circle of reflexes, which does not at once reestablish itself. This possibility will be referred to subsequently.

When injections of procaine hydrochloride near the second to the seventh thoracic sympathetic ganglion are successful in relieving phantom limb pain the sequence of objective and subjective changes that ensues is little short of miraculous to the patient and the observer alike. The pain disappears; an increasing sense of warmth and relaxation pervades the cramped extremity, and one by one the fingers open and can be moved voluntarily. The relief of pain, with its associated peripheral vasodilatation, is so consistent that one cannot escape the conclusion that impulses conveyed by the sympathetic nerves, either efferent or afferent, must have been contributing to the painful phenomena.

It would not be difficult to explain the relief of pain if it were known definitely that the sympathetic pathways transmit painful sensation from the arm. A few careful observers, such as Foerster,¹⁰ Reschke¹¹ and

10. Foerster, O.; Altenburger, H., and Kroll, F. W.: Ueber die Beziehungen des vegetativen Nervensystems zur Sensibilität, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **121**:139-185, 1929. Foerster, O.: Ueber das Phantomglied, *Med. Klin.* **122**:497-500, 1931.

11. Reschke, K.: Lumbar Ramisection for Causalgia in an Amputation Stump of the Thigh, *Internat. Abstr. Surg.* **59**:504-505, 1934.

Shaw,¹² have asserted that pain impulses from the periphery do traverse the sympathetic ganglions. Many of the data tending to indicate that afferent neurons may enter the sympathetic chain by way of the gray rami from the mixed nerves or by following major blood vessels proximally have been secured in a study of human subjects under clinical conditions. The surgical clinic has obvious disadvantages for the conduct of controlled experiments, but in a study of so subjective a phenomenon as pain it may be a more fertile source of information than the laboratory. At least, some of the clinical observations, such as the undeniable benefits occasionally conferred by periarterial sympathectomy, are most difficult to affirm or deny on the basis of animal experimentation. However, the great weight of experimental evidence is against the opinion that pain impulses from the periphery traverse the sympathetic ganglions. It indicates, rather, that they follow the mixed nerves, to enter the spinal cord by way of the posterior roots of the brachial plexus.

If one concedes that the relief of pain is not due to an interruption of afferent pathways, it is apparent that the effect must be attributable to an abolition of vasomotor impulses which have been contributing to the production of pain. Leriche¹³ suggested in 1927 that relief of peripheral pain obtained by section of sympathetic fiber tracts might be due to some alteration of the blood supply acting on pain receptors of the somatic nerves. In the same year Sfameni and Lunedei¹⁴ elaborated a somewhat similar theory. A more recent presentation of this same idea has been advanced by Davis and Pollock¹⁵ in their discussions of "referred pain." That the vasomotor effects responsible for the phenomena of pain act on receptor *end organs* of somatic sensory neurons is implied by the following quotation from their paper:

The impulses travel over preganglionic efferent fibers to the autonomic ganglions. A postganglionic fiber then carries the impulse to the skin, where sensory end organs are stimulated. Thus an ordinary somatic painful impulse is produced which travels over the spinal sensory nerves, enters the spinal cord by way of the posterior roots, and ascends in the lateral spino-thalamic tract to a cortical level.

It is difficult to make this theory apply to cases of phantom limb pain. The patients with this condition feel pain of specific quality and localiza-

12. Shaw, R. C.: Sympathetic System and Pain Phenomena, *Arch. Surg.* **27**:1072-1080 (Dec.) 1933.

13. Leriche, R.: Recherches et réflexions critique sur la douleur, *Presse méd.* **35**:497-499, 1927.

14. Sfameni, P., and Lunedei, A.: Sui refessi viscerocutanei e sul meccanismo di produzione del dolore nelle affezioni dei visceri e delle sierose, *Riv. di clin. med.* **28**:758-766, 1927.

15. Davis, L., and Pollock, L. J.: The Rôle of the Autonomic Nervous System in the Production of Pain, *J. A. M. A.* **106**:350-353 (Feb. 1) 1936.

tion. It is relieved by interruption of the sympathetic pathways, but in this instance there are no sensory end organs in the parts where the pain is felt to originate. Since the limb has long since been amputated, it follows that pain ascribed to a particular finger cannot be due to any physiochemical changes in that finger acting on pain receptors of somatic sensory nerves.

One might assume that nerve fibers as well as end organs are capable of originating specific pain sensations when an adequate stimulus is supplied. When a sensitive neuroma is pinched a shocklike flash of pain may be felt in the area normally supplied by that nerve trunk, but such a pain has few of the characteristics of true fantom limb pain. A sensation similar to that produced by pinching a neuroma is caused by electrical or mechanical stimulation of exposed fiber bundles of mixed nerves, but there are lacking the specific characteristics of heat or cold, "tension," "tearing," "rawness" or "cutting" observed in fantom limb pain, and the pain is not referred to a particular part of a single digit. Attempts to stimulate a few fibers or even a single fiber have thus far failed to produce a specific or localized sensation. Yet it is possible that under experimental conditions the stimulus has not been adequate in quality and intensity, and that physicians have been led to the erroneous conclusion that specific sensations cannot originate in nerve fibers (in much the same way in which early investigators of visceral sensation were influenced to conclude that the viscera were entirely lacking in pain sensibility because they did not respond with sensations of pain to trauma or to thermal or chemical stimuli). Certainly it is difficult to avoid the conclusion that, whatever the pathologic physiology of fantom limb pain may be, the underlying exciting cause is to be found in the amputation stump. By no other means is it possible to account for the temporary alleviation of pain by compression of the arm with a sphygmomanometer cuff or by direct pressure over the principal artery; nor is it possible to account otherwise for the interval of relief from pain that may follow the resection of nerves or blood vessels or even the infiltration of the stump with a local anesthetic.

One can only speculate as to whether the trouble in the fibers is caused by compression of nerve trunks by scar tissue, by anoxemia and impaired nutrition, by direct stimulation of afferent neurones in the walls of damaged blood vessels or by some unknown physiochemical agent. Regardless, however, of the other factors which may aid in producing the syndrome of typical fantom limb pain, the nerve fibers in the stump undoubtedly are the ultimate exciting cause.

This point is well brought out in a study of the relation of the syndrome of fantom limb pain to other pain syndromes which suggest that nerve fibers have been irritated. I have in mind particularly *causalgia* (*thermalgia*), but there are also suggestive points of similarity to the

cervical rib syndrome, Volkmann's ischemic paralysis, the "protopathic" phase which may accompany nerve regeneration, and certain post-traumatic disturbances characterized by intractable pain.

In the irritative lesions of peripheral nerves there is usually observed a characteristic combination of symptoms. The pain is spontaneous and peculiarly unbearable; it tends to radiate; there are frequently associated sensations of cold or burning heat; hyperesthesia is almost invariably present; and, most striking of all, there occur vasomotor, sudomotor and trophic changes which indicate that reflexes involving the visceral nervous system have been called into play. Usually the disability which accompanies the irritative neural lesion is far greater than that which occurs when the nerve has been completely divided. This fact might be used to argue against the essential similarity of these conditions to phantom limb pain, because in patients suffering from such pain the nerves have, of course, been completely severed; but it does argue that lesions which involve nerve fibers are capable of setting off a train of serious and disabling symptoms.

I say "setting off a train of symptoms" because I believe that the initial lesion is merely the percussion cap that leads to the detonation of the main powder cache. In a former writing³ I said: "It seems probable that the injury to certain tissues starts a cumulative process which is not confined to the single nerve distribution and which tends to spread to involve the spinal cord in diffuse reflex phenomena in which the sympathetic nerves are prominently affected." The interval of time that frequently elapses between the injury and the onset of the pain, the period of relief that may follow the division of nerves at higher levels and the increasing momentum of all the associated phenomena suggest that a vicious circle of reflex activity is present. Unquestionably, the sympathetic nerves form an important link in the vicious circle. Once the sympathetic nerves are involved, anything that adds to their activity, whether it be emotional distress, cold, barometric alterations or local injury, may augment the pain. Conversely, anything that lessens their activity, such as mental equanimity, physical relaxation, warmth and comfort, or careful guarding of the part, may diminish the intensity of the pain. Finally, anything that interrupts the sympathetic component of impulses may break the vicious circle temporarily. If the break is complete, a considerable period of time may elapse before the circle is established in its original intensity and the centers of the spinal cord and the brain are involved. If the circle is repeatedly broken, it may never reestablish itself effectively. I believe that in this rather vaguely expressed concept may lie the explanation of the fact that repeated injections of procaine hydrochloride near the sympathetic ganglions have "cured" phantom limb pain in some cases.

It is possible that, as Leriche¹ has suggested, a certain "tissue susceptibility" in particular persons (just as some patients have a tendency to keloid changes in surgical scars while others have not) may be a factor in determining whether with irritative neural lesions they will have causalgia or whether after having an amputation they will suffer phantom limb pain. Without doubt, the temperament of the patient has much to do with his reaction to pain. It is also possible that showers of afferent impulses from the periphery may hypersensitize the spinal cord or the brain centers, or that garbled messages from the stump may be misinterpreted by the thalamic centers, so that, as Stopford¹⁶ has suggested in the case of protopathic pain, there may be overreaction and exaggeration. Yet it seems to me wholly unreasonable to conclude that because a particular patient suffers from causalgia or phantom limb pain while another with an apparently similar lesion does not the patient with painful symptoms is therefore neurasthenic and his trouble is not amenable to any but psychic therapy. There should be sympathy and understanding as well as unsparing effort to relieve the suffering of these unfortunate persons, even though physicians' insight into the mechanisms responsible for the pain is still obscured.

SUMMARY

The syndrome of phantom limb pain is a definite clinical entity.

Its symptoms may be temporarily alleviated in many instances by injections of procaine hydrochloride in the region of the thoracic sympathetic ganglions.

Occasionally, the relief afforded by such an injection persists for a long time.

The observations here reported suggest that the present interpretation of the influence of the sympathetic nerves on pain of peripheral origin may require modification.

16. Stopford, J. S. B.: *Sensation and the Sensory Pathways*, London, Longmans, Green & Co., 1930.

OSTEOMYELITIS OF THE PELVIC GIRDLE

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Like all other bones of the skeleton, the component parts of the pelvic girdle are subject to the occurrence of foci of osteomyelitis. It is found that the forms of osteomyelitis usually resulting from or associated with various kinds of trauma are more prevalent than the orthodox hematogenous forms resulting as thromboembolic phenomena in the course of a general infection (sepsis, pyemia or bacteremia).

ANATOMY

The pelvic girdle is composed of two main divisions: (1) the sacrum¹ and (2) the innominate bone. The sacral vertebrae conform in structure, external form and physiologic function with the other bones of the spine, except that they are fused during adolescence to form the adult entity known as the sacrum.

The innominate bone is one of the most irregular bones of the body. The external physical form of its major segments resembles that of all the other bones of the skeleton, including the long bone, the flat bone and the irregular bone proper. Nevertheless, its intimate structure is essentially that which is seen in the true irregular bone, such as the vertebra or the maxilla, and consists of an outer thin plate of compact osseous tissue surrounding and enclosing an interior mass of cancellous tissue. Nowhere is there a suggestion of a marrow cavity. In the parts where function demands broad surfaces and a thin platelike structure, the cancellous tissue disappears entirely, and only the two opposing layers of compact bone tissue remain, fused in a thin plate. This is especially noticeable at the bottom of the acetabulum and in the center of the iliac flare. During the development of an osteomyelitic focus perforation of these thin parts of the bone is relatively common.

The entire structure is covered by a well developed periosteum (to which the various muscles are attached) except for certain areas. Along the crest of the ilium, over the anterior and especially the posterior iliac spine and over the anterior surfaces of the rami of the pubis

1. As the subject of osteomyelitis of the spine has been thoroughly discussed on another occasion, I shall not include any extensive discussion of osteomyelitis of the sacrum in this communication except where it is found necessary because of its association with osteomyelitis of the innominate bone proper.

and the ischium the attachment of the muscles makes for deep anchorages, which disturb somewhat the distinctness of the individuality of the periosteal membrane. This is necessary because of the physiologic function of these muscles. At the symphysis pubis and at the sacroiliac synchondroses the periosteum disappears and is replaced by a thin layer of cartilage; the entire structure at these areas is surrounded by thick ligamentous layers.

The Blood Supply.—The blood supply of the pelvic girdle comes from the periosteal plexus, which is formed by a number of supply vessels perforating the periosteal layers at various points. A distinct nutrient vessel commonly perforates the outer side of the ilium between the crest and the anterior and posterior gluteal lines. On the inner side the iliac branch of the inferior gluteal artery perforates the bone under cover of the iliacus muscle.

The obturator artery passes forward and downward on the lateral wall of the pelvis to the upper part of the obturator foramen. Inside the pelvis it gives off iliac branches to the iliac fossa, which supply the bone and the iliacus muscle; it has also a pubic branch, which ascends on the back of the pubis, communicating with the corresponding vessel of the opposite side and with the inferior epigastric artery. Outside the pelvis the obturator artery, by its posterior branch, follows the posterior margin of the foramen and turns forward on the inferior ramus of the ischium, where it anastomoses with the anterior branch. It supplies an articular branch which enters the hip joint through the acetabular notch, ramifies in the fat at the bottom of the acetabulum and sends a small branch along the ligamentum teres to the head of the femur. The internal pudendal artery gradually approaches the margin of the inferior ramus of the ischium and passes forward between the two layers of the fascia of the urogenital diaphragm; it then passes forward along the medial margin of the inferior ramus of the pubis.

According to Lexer, Kuliga and Turck, the most important part of the blood supply goes to the ilium. The most important vessel perforates the inner side of the ilium near the posterior end of the arcuate line and proceeds forward, upward and anteriorly toward the flare of the bone. Many branches proceed toward the iliac crest. Relatively large vessels supply the upper ramus of the ischium and proceed backward in the general direction of the sacroiliac synchondrosis. Little change in the arrangement of the blood vessels occurs as the person grows older.

The blood supply is at a minimum where the bone is thinnest and consists of compact bone solely; it varies in other parts of the bone with the extent of the cancellous structure, and in young persons it is most abundant in and around the centers of ossification. Here the

vascular loops are to all intents and purposes end vessels. The most abundant supply is in the general neighborhood of the acetabulum and the junction of the three segments of the innominate bone. Clinically this corresponds to the more frequent localization of foci of osteomyelitis in these areas.

An extraordinary fact in this ensemble is the relatively small blood supply as compared with that of other bones. Possibly this is the most important single factor which contributes to the relatively small number of foci of osteomyelitis which occur in the pelvic girdle, for poverty of vascular channels would give small opportunity for the establishment of thromboembolic foci.

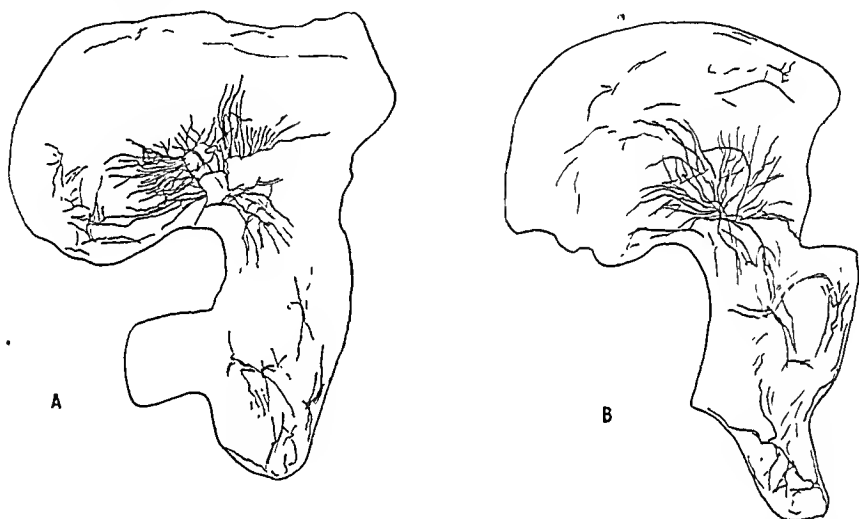


Fig. 1.—Blood supply of the innominate bone; semidiagrammatic, after E. Lexer, P. Kuliga and others (*Untersuchungen mittelst Röntgenaufnahmen injizierter Knochen und ihre Bedeutung für einzelne pathologische Vorgänge am Knochensysteme*, Berlin, A. Hirschwald, 1904). *A*, view sketched from the outer side of the bone. *B*, view sketched from the inner side of the bone.

Development and Ossification.—According to Gray's "Anatomy":

. . . the hip bone is ossified from eight centers: three primary—one each for the ilium, ischium, and pubis; and five secondary—one each for the crest of the ilium, the anterior inferior spine, the tuberosity of the ischium, the pubic symphysis and one or more for the Y-shaped place at the bottom of the acetabulum. . . . At birth, the three primary centers are quite separate. The others . . . being still cartilaginous. By the seventh or eighth year, the inferior rami of the pubis and ischium are almost completely united by bone. About the thirteenth or fourteenth year, the three primary centers have extended their growth into the bottom of the acetabulum, and are there separated from each other by a Y-shaped portion of cartilage, which now presents traces of ossification, often by two or more centers. One of these, the os acetabuli, appears about the age

of twelve, between the ilium and pubis, and fuses with them about the age of eighteen; it forms the pubic part of the acetabulum. The ilium and ischium then become joined, and lastly the pubis and ischium, through the intervention of the Y-shaped portion. At about the age of puberty, ossification takes place in each of the remaining portions, and they join with the rest of the bone between the twentieth and twenty-fifth years. Separate centers are frequently found for the pubic tubercle and ischial spine, and for the crest and angle of the pubis.

Clinically, the various centers of ossification are important because terminal loops (that is, end arteries) are present in the areas surrounding the centers of ossification. They form points of election for the formation of thromboembolic foci, and in actual practice foci of osteomyelitis are found to develop most frequently in these areas and in association with the abundant vascular plexus found in the neighborhood of centers of ossification.

Physiology and Function.—The most important function of the pelvic girdle is mechanical; the bone serves to transmit the weight of the trunk and the upper limbs to the lower extremities. The underlying principle of the general architecture of the pelvic girdle is that of the arch. The obliquely lateral curve of the innominate bone proper corresponds to the sides of the arch, and the sacrum corresponds to the keystone. The various stresses and strains are so disposed that the lines of force also correspond to a series of arches obliquely superimposed one on the other. In this way the maximum amount of physiologic purpose is achieved with a minimum of structural material. In order to lessen concussion in rapid changes of distribution of the weight, the sacroiliac articulations are interposed between the sacrum and the iliac bones, and the pubic symphysis exists in the middle of the anterior arch.

During pregnancy the pelvic joints and ligaments are relaxed and are therefore capable of extensive movements. When the fetus is being expelled the force is applied to the front of the sacrum. Upward dislocation is again prevented by the interlocking mechanism of the middle segment. As the fetal head passes the anterior segment the latter is carried upward, enlarging the anteroposterior diameter of the pelvic inlet; when the head reaches the posterior segment this also is pressed upward against the resistance of its wedge, the movement being possible only by the laxity of the joints and the stretching of the sacrotuberous and sacrospinal ligaments.

CLASSIFICATION OF FORMS OF OSTEOMYELITIS FOUND CLINICALLY

Primary, extension and hematogenous forms of osteomyelitis occur in the bones of the pelvic girdle. As a general rule, the number of cases of the primary and extension forms of osteomyelitis exceeds

the number of those in which the condition is due to hematogenous infection. Frequently there is a certain amount of association of the mechanisms causing the primary and extension forms, so that it is difficult clinically to differentiate accurately between the two. The difficulty exists especially with conditions occurring after trauma or after a surgical operation. When the physical objective signs of the infection of bone occur immediately there is little doubt that the process is a primary osteolytic infection. When some time elapses between the operation and the demonstration of the osteomyelitic process, one of two explanations is possible: 1. The process may have started immediately but with so few subjective and objective symptoms that the infection of the bone was not observed until it had passed into the chronic stage. Such a process is still a primary infection of bone, that is, primary osteomyelitis. 2. Infection may have developed in the soft parts and a steady progression of the process occurred until the bone was secondarily involved and the condition was recognized clinically some time later. This is the extension form of osteomyelitis. The following description of the primary and extension forms of osteomyelitis of the pelvic girdle is made with this reservation in mind.

In cases of hematogenous infection there is practically never any difficulty clinically in determining the pathogenic origin.

PRIMARY OSTEOMYELITIS OF THE BONES OF THE PELVIS

Primary osteomyelitis of the pelvic girdle is always a consequence of trauma and necessarily follows the production of an open wound which communicates with the bones. Though a gross fracture is usually demonstrable, it is not necessarily so; a stab wound may traverse the overlying soft parts and penetrate the bone, or a bullet may cause a groove in the surface of the bone. In compound fractures the communication may extend to the skin, to the interior of the bladder or bowel or to the surface of the vagina. In civil life the commonest form of compound fracture extends into the bladder; in comparison with this, compound fracture into the skin or into the rectum is uncommon. Communication with the vagina is somewhat more common. Primary or secondary infection of the bone as a consequence of compound fracture into the bladder is most unusual, because operation is almost always immediately necessary and modern technic requires closure of the bladder wound and drainage of the bladder through the urethra by catheter. If because of the situation of the bladder rupture (for example, if it occurs at the neck of the bladder) immediate closure of the bladder is impossible, the drainage of urine is established by the suprapubic route; the extension form of osteomyelitis occasionally follows, as will be pointed out later.

In both civil and military traumas of large degree, as, for instance, when a fall from a great height causes extensive shattering of the pelvic girdle with compounding of the fracture either externally or internally, or in wounds caused by shrapnel and shell with equally extensive loss of tissue, the injury is commonly of such importance as to cause death either immediately or very shortly. Under such conditions, osteomyelitis does not have any opportunity to develop.

In civil and military life wounds produced by similar objects (that is, bullet wounds and stab wounds) are essentially similar. Troops in active engagement, however, are handicapped by fatigue, by undernourishment, by the filthy conditions of field warfare, by the extraordinary likelihood of fecal contamination of any and every wound, by the frequent inclusion of foreign bodies (for example, pieces of clothing) in the wound and by delay in receiving adequate medical and surgical attention.

The treatment for these forms of injury is essentially prophylactic and is planned to prevent infection of any kind in any part of the tissues involved in the injury; naturally, this also includes the prevention of any infection in the osseous tissue. In differentiating between the injuries occurring in civil life and those occurring in military life it will be found that the necessary débridement is more extensive with the latter class of injuries than with the former. Except for this the treatment, prophylactic and otherwise, is the same in either class. In cases of injuries communicating with the intestinal tract it is advisable to administer prophylactic doses of gas gangrene and tetanus antitoxin.

Primary infection of the pelvic girdle complicates operations on the bone itself, on the tissues in contact with it or on the organs housed in the pelvis when the surgical procedure necessitates baring of the osseous structure or resection of portions of it. The two commonest varieties of infection occur with operation for sacral dermoid cyst and with the sacral or perineal type of operation for carcinoma of the rectum.

Osteomyelitis Following Operation for Excision of Sacral Dermoid Cyst.—I have seen several persons in whom a superficial form of osteomyelitis of the sacrum followed excision of an infected sacral dermoid cyst. Clinically these infections of the bone served to inhibit the healing of the wound for a much longer period than was normal. In no instance was a revision of the wound found necessary.

Osteomyelitis Following the Sacral Type of Operation for Carcinoma of the Rectum.—In the sacral (Kraske) and in the perineal form of operation for carcinoma of the rectum all the factors just referred to are present. A common postoperative complication is a necrotizing infection of the soft tissues attached to the sacrum. This infection

occasionally is extensive enough to pass around the great sacrosciatic notch and involve the ilium; the necrotized tissues become black, and gas is frequently produced. When the patient is able to withstand the immediate effects of the operation and the subsequent effects of the intense necrotizing inflammation, the eventual separation of the dead and sequestrated tissue commonly reveals that the infection has passed into the underlying bone, and frequently small sequestrums are extruded.

In the sacral operations and in a few of the perineal operations in which the coccyx alone is excised, there is usually an immediate infection of the bone at the line of section. Some, at least, of the extraordinary length of time necessary for the healing of the wound undoubtedly must be referred to the infection of the bone.

The infection found complicating perineal operations is undoubtedly an immediate infection, or primary osteomyelitis. The type of infection which complicates sacral operations partakes of the mechanism of both primary and secondary infection of the bone.

The treatment of either of these forms of osteomyelitis when the condition occurs as a complication of operation is conservative.

EXTENSION FORMS OF OSTEOMYELITIS OF THE PELVIC GIRDLE

Extension forms of osteomyelitis of the pelvic girdle also follow as a complication of the clinical events outlined in the previous sections. In clinical practice the following varieties are found in addition.

Osteomyelitis of the Pubis Following Suprapubic Cystotomy.—In this clinical syndrome there is apparently a mild form of infection customarily indicated by the term "periostitis" or "osteitis." It occurs after operations in which the bladder is opened, and subsequent urinary drainage occurs through a suprapubic fistula for the usual considerable length of time. The operations are commonly done for hypertrophy of the prostate, for malignant tumor and occasionally for stone. The development of the pathologic process in the bone is aided by the necrotizing effect of the irritating and infected urine on the soft tissues attached to the symphysis pubis. The bone is secondarily bared and infected after the separation from it of the necrotic soft tissue. In this extension condition infection in the osseous tissue is aided by injury to the periosteum or to the bone, by continued traction of the muscles attached to the bone and most of all by necrosis of the margins of the drainage tract caused by pressure of the tube or other drainage apparatus. Diabetes when it exists is a powerful adjuvant factor. In cases in which a malignant lesion is present the undernourished condition of the tissues is also an important factor.

In the literature there are only a few references to this complication of suprapubic cystotomy. There are references to it by Cabot in his

"System of Urology," by Lazarus² and by Beer.³ Beer's paper from the Mount Sinai Hospital, New York, includes reports of 3 cases in which the condition was positively identified and a reference to "numerous other similar cases." Lazarus' experience included the observation of 3 cases. In 1 of these the lesion was proved roentgenologically to be extensive. This should not mislead any one into taking it for granted that this complication is rare. It is so easy to fail to recognize the clinical fact of this lesion's occurrence in what may be a large, foul and badly infected wound that many more such lesions actually occur than are recognized or reported. The extensive lesions are recognized; the lesser ones, lesser both in extent and in clinical disturbance of postoperative convalescence, are lost because of the physician's negligence or because of his inability to recognize the subjective and objective symptoms.

The clinical picture of this complication is usually definite. Because of the situation of the osteomyelitis in the symphysis, the pubis and the neighboring rami, the outstanding symptoms are pain over the lower attachments of the rectus abdominis muscle, over the body, symphysis and rami of the pubic bone and over the inner aspects of the thighs with spasm of the adductor muscle, so that the patient finds it painful to walk, to spread the thighs and to cough. Late symptoms are pain on defecation and terminal dysuria. Fever may be present in the early stages of the complication, but even then it may not be properly referred and integrated because of the original disease and operation. Any supuration referable to the osseous lesion is unrecognizable clinically in the usual discharge from the wound, diluted as it always is in the escaping urine (see section on hematogenous osteomyelitis of the pubis).

In the early stages of the lesion roentgen examination may yield entirely negative results or may reveal an inconclusive fraying of the edges of the bone. In extensive lesions in a later stage there are definite areas of absorption which leave little doubt that some extensive lesion has occurred. In the absence of a malignant condition the diagnosis can be definitely made of an inflammatory lesion, that is, osteomyelitis. In the presence of a malignant condition the diagnosis is not quite so simple, and differentiation must be made from metastatic deposits in the bone. Also, it is conceivable that the two lesions may coexist.

Osteomyelitis of the pubis is usually a self-limited complication of suprapubic cystotomy. The treatment should usually be palliative, expectant and conservative. Naturally, the sinus will not close until the condition of the bone is normal, but in the reported cases a permanent fistula has rarely, if ever, occurred. In cases in which the lesion

2. Lazarus, J. A.: *Ann. Surg.* **103**:310, 1936.

3. Beer, E.: *J. Urol.* **20**:233, 1928.

is extensive sequestration may take an untoward length of time, and in some the time of healing and convalescence may be shortened by revision of the wound. Ordinarily the time of healing varies, according to the extent of the lesion, from two to six months.

Osteomyelitis of the Pubis Occurring After and Complicating Symphysiectomy in Obstetric Cases.—In a review of the literature up to 1934 Jentzer⁴ could find only 1 case of this kind. None of several obstetricians whom I consulted could recall a similar case in his experience. Jentzer's experience consists of the observation of a single case.

Jentzer's patient, a woman aged 29 who had never been seriously ill, was subjected to symphysiectomy during a difficult delivery. About two weeks later she complained of pain in the pelvis, and there was a discharge from the wound over the symphysis. When she began to walk she felt agonizing pain in the region of the pubis, and her gait resembled that caused by bilateral congenital dislocation of the hip. Her condition gradually became worse. About five months after the delivery, when she was first seen by Jentzer, roentgen examination of the pubis showed separation of the symphysis for about 20 mm., destruction of bone, rough edges and small sequestrums. Operation was followed by complete recovery.

I was able to find an additional case in the records of Söderlund.⁵

In Söderlund's case the patient was a woman who had had an uncomplicated labor and who complained thereafter of pain radiating down the right lower extremity which continued during the puerperium. The pain increased progressively during the next one and one-half years, and eventually it also radiated to the right hip. A vaginal discharge appeared early, continued and was finally traced to a sinus which communicated with the os pubis. This led to the correct diagnosis. After sequestrotomy the symptoms promptly subsided.

HEMATOGENOUS OSTEOMYELITIS OF THE PELVIC GIRDLE

Except for its location and some factors peculiar to this location, hematogenous acute osteomyelitis of the bones of the pelvic girdle differs in no way from similar forms of osteomyelitis in any of the other bones of the skeleton. All the facts applying to the etiology, bacteriology, mechanism of infection, pathology and pathogenesis which I have described and discussed on many previous occasions, and have also included in my book,^{5a} apply to hematogenous acute osteomyelitis of the bones of the pelvis.

The groups of reported cases found in the literature are summarized in table 1.

The Mount Sinai Hospital series contained 346 cases of osteomyelitis of all types and of all the bones of the skeleton. The patients were

4. Jentzer, A.: *Rev. d'orthop.* 21:289, 1934.

5. Söderlund, G.: *Acta chir. Scandinav.* 67:850, 1930.

5a. Wilensky, A. O.: *Osteomyelitis: Its Pathogenesis, Symptomatology and Treatment.* New York, The Macmillan Company, 1934.

admitted to the hospital between 1926 and 1932. There were 12 cases of hematogenous osteomyelitis of the pelvic bones. The distribution is shown in table 2. I have had 1 private case of hematogenous osteomyelitis of the ilium in which the condition occurred in a patient with

TABLE 1.—*Cases of Hematogenous Osteomyelitis of the Pelvis Reported in the Literature*

Author	Location of Lesion	Number of Cases	Total Cases Osteomyelitis	Total Lesions
Klemm, P.: Die akute und chronische infectiöse Osteomyelitis des Kindesalters auf Grund eigener Beobachtungen und Untersuchungen, Berlin, S. Karger, 1914	Ischium Pubis	2 2	320	385
Lloyd, E.: Proc. Roy. Soc. Med. 21: 1387, 1928	Pubis and Ischium	2	29	
Ogilvie, W. H.: Proc. Roy. Soc. Med. 21: 1390, 1928	Pubis	1	51	
Platt, H.: Proc. Roy. Soc. Med. 21: 1378, 1928	0	41	
Doran, W. T., and Brown, L.: Surg., Gynec. & Obstet. 40: 658, 1925	Ischium	3	71	
McWhorter ¹⁰	Pubis and Ischium	1 3		
Racshke: Klin. Wehnschr. 7: 72, 1928	Pubis	1		
Phemister, D. B., cited by McWhorter ¹⁰	Pubis	1		
Kulowski ⁶	Sacrum and ilium	9		
Iseu ⁷	Pubis	3		

TABLE 2.—*Location of Pelvic Bone Lesion in Cases of Hematogenous Osteomyelitis.*

Location of Lesion	Cases	Total Lesions
Pubis.....	1	3
Bilateral pubis (symphysis).....	1	
Ilium.....	5	
Ilium and bilateral pubis (symphysis).....	1	4
Ischium.....	2	
Sacrum.....	2	2

TABLE 3.—*Age Distribution in Cases of Hematogenous Osteomyelitis*

Age	Number of Patients
1 to 10 years.....	2
11 to 20 years.....	4
21 to 30 years.....	1
31 to 40 years.....	0
41 to 50 years.....	1
51 to 60 years.....	4

two other osteomyelitic lesions. There were 7 male and 5 female patients in the series of 12 cases. The age distribution is shown in table 3. It seems a little extraordinary that 5 of the patients should have been above 30 years of age; this is a variation from the age incidence in cases of hematogenous osteomyelitis of the other bones of the skeleton.

Bacteriologic studies are available in 2 of these 12 cases. In 1 case the lesions yielded *Staphylococcus aureus*; in the other they yielded *Streptococcus haemolyticus*. In both of these cases the blood culture was positive.

Pathogenesis and Pathology.—The pathologic picture, pathogenesis and mechanism of hematogenous acute osteomyelitis in the pelvis are exactly similar to those of the same condition in the other bones of the body and are based on the formation of a thromboembolic lesion in the vascular plexus of the bone. Because of the essential anatomic and vascular conditions there is no repetition of the typical distribution seen in the long bones, and the lesions produced in the pelvic bones are of irregular size and shape and are determined by the anatomic arrangement of the blood vessels. In the pubis and ischium the lesions vary from concentration in inconsequential segments to involvement of nearly the entire anatomic segment. In the ilium the lesions most often are in the neighborhood of the acetabulum or along the crest; in the flare of the ilium complete development of the lesion is commonly followed by oval or circular deficiencies in the bone structure. Periosteal lesions are as common as lesions involving the entire thickness of the bone.

General Symptoms.—The general symptoms and course of acute hematogenous osteomyelitis of the bones of the pelvis differ in no way from those present when the disease attacks other bones of the skeleton. This is especially exemplified when multiple lesions are present and when one or more of these are located in the pelvis. The several classifications into hyperacute and moderately severe infections obtain in cases of pelvic localization as well as in others.

In the hyperacute condition the clinical picture is that of a profound and overpowering infection and intoxication of the entire system. There are initial chills and subsequent high fever, and the general condition rapidly becomes alarming. Blood cultures are positive as a rule. The signs of any local disease are at a minimum, are frequently absent, and when present and looked for are not easily demonstrable, owing to the tremendous intoxication which is present. With the most severe forms death follows in a few hours from the general infection. From the severe and dramatic forms, all grades of intensity of infection exist, down to those described in the following sections.

In cases in which the condition is very severe the diagnosis is frequently in doubt beyond the bare fact of the presence of a general infection. Erroneous diagnoses are common: frequently the disease is assumed to be typhoid fever, or because the character of the symptoms is influenced by the rapid development of some complication within the meninges it is thought that cerebrospinal meningitis is present. Examples of this kind are numerous in the literature.



Fig. 2.—Perforation of the flare of the ilium after osteomyelitis.



Fig. 3.—Osteomyelitis of the flare of the ilium extending down to the acetabulum.
(Supplied by Dr. Farr.)

The differentiation of osteomyelitis from other diseases is not, moreover, the sole diagnostic difficulty. It is also extremely difficult to determine whether the osteomyelitic focus exists in those segments of the innominate bone which are anatomically distant from the iliac flare and crest, whether it is located in the hip joint or whether it is to be found in the head or neck of the femur. Even when local symptoms of pain and tenderness, general tumescence and limitation of motion are present this difficulty is not lessened. Roentgenographic studies do not give any indication of the location in the first ten days of the infection and are therefore of no help. An illustrative case is the following one from the records of the Mount Sinai Hospital:

A boy was admitted with symptoms of a severe infection and with local signs pointing to the general region of one hip. Because it was not possible to locate the focus accurately, I decided to follow the conservative method of treatment and not to operate. This treatment gave satisfactory results, and operation was never done. Several months later there was roentgenographic and clinical proof that the focus was in the lower ramus of the pubis. The possibility of this localization had not occurred to me or to any of my associates at the time the patient was admitted to the hospital.

Local Symptoms.—The local signs present special characteristics according to the segment of the pelvic girdle which is involved. These may be referred (1) to the sacrum, (2) to the sacroiliac region, (3) to the flare of the ilium, (4) to the central acetabular region, (5) to the pubic bone or (6) to the ischium.

I. HEMATOGENOUS OSTEOOMYELITIS OF THE SACRUM

At an early stage of hematogenous osteomyelitis of the sacrum the patient shows a tendency to assume the supine posture. Tenderness and rigidity of the lower end of the spine are present. In a few days the following local signs point to the actual seat of disease:

Local Swelling.—When the lesion is in the posterior aspect of the sacrum the signs consist in the development of a widespread and indefinitely demarcated edematous swelling and tenderness over the appropriate part of the sacrum. The swelling is usually not detected before the third or fourth day, and in some of the recorded cases it was detected even later. A striking characteristic is the widespread area of the soft parts affected as compared with the extent of the affected area in the bone.

When the process is in the anterior part of the bone and shows a tendency to point anteriorly, there is little, if any, external evidence of the existence of infection in the bone. In cases of severe involvement the nature of the illness is lost, and a diagnosis of typhoid fever or of meningitis is often made; in some cases, indeed, the true diagnosis

is made only after death. Rectal examination is the most important part of the physical examination. The elicitation of tenderness and the palpation of the subperiosteal abscess which invariably forms in the hollow of the sacrum should lead to a correct diagnosis.

Local Pain.—In cases in which the condition is less severely toxic pain is an important symptom. The pain is of two kinds, spontaneous and provoked. Spontaneous pain varies in different cases. Pain provoked by pressure over the affected area has great diagnostic value and permits the location of the process to be determined at a relatively early stage of the disease.

II. HEMATOGENOUS OSTEOMYELITIS OF THE SACRUM AND ILIUM SURROUNDING THE SACROILIAC JOINT

Attention has recently been called to the form of hematogenous osteomyelitis which is found in the ilium and sacrum surrounding the sacroiliac joint. Kulowski's⁶ report discussed an incidence of approximately 30 cases in Steindler's clinic in the State University of Iowa. The report is somewhat obscure, because it is difficult to distinguish from the descriptions given whether the process began in the joint, in the sacrum or in the ilium; furthermore, Kulowski spoke of "osteomyelitis of the sacroiliac joint," which is obviously a misnomer.

The following are the pathogenic possibilities:

A. The process may begin as an infection solely of the joint. It is a common experience to find clinical evidence of disease in the joint but roentgenographic evidence proving that there is no involvement of any part of the bone contiguous to the joint. In most lesions of this origin the bone remains uninvolved.

B. The process may begin in the bone, either in the sacrum or in the ilium. Involvement of the joint occurs secondarily. Kulowski stated that once the joint is involved extension occurs rapidly and almost inevitably from one bone to the other, making the lesion a total one, and that this is the usual progression of the lesion.

C. The vascular lesion may be such as to involve the joint and the bone simultaneously.

By the time the lesion is definitely established and clinically recognized, both joint and bone are usually involved. Destruction of osseous tissue in the sacrum is much more serious, functionally, than is similar destruction in the ilium. From Kulowski's report it appears that sclerotization readily occurs in the thin plate of the iliac flare and limits to a certain extent the spread of the lesion in that direction.

6. Kulowski, J.: *Am. J. Surg.* 23:305, 1934.

Symptoms.—A careful history should not fail to call attention to the general region of the sacroiliac joint. The rapidity of onset and the development of the subjective and objective symptoms vary with the individual patient. Pain is always present and is not usually relieved by any change of posture. There may be radiation of the pain along the sciatic distribution, and in some cases it is referred to the hip. Spasm of the iliopsoas muscle is present. Objectively the extent and principal location of the lesion are difficult to determine. Except in the presence of an external accumulation of pus, the external tissues merely show



Fig. 4.—Osteomyelitis of the sacroiliac region. This is the extension form of osteomyelitis. (Supplied by Dr. Frank E. McIneny.)

edematous induration. Tenderness over the joint and the adjacent parts is marked.

Retroperitoneal irritation is frequently present. It shows itself by spasm of the iliopsoas muscle and by symptoms referable to the bowel and to the lower segments of the genitourinary tract.

Roentgenographic study usually reveals no definitive data in the early stages of development of the lesion. Later there are abundant evidences of more or less destruction of osseous tissue and disorganization of the sacroiliac joint, and when the lesion is unilateral the differences are striking.

Formation of Abscesses in Sacral and Sacroiliac Osteomyelitis.—

Abscesses and abscess extensions of the most bizarre type may develop, and these tend sometimes to mislead the physician as to the site of the original focus. According to the location of the lesion, abscesses may occur on the anterior or posterior aspect of the bone or, more rarely, on both, and sometimes suppuration occurs in the interior of the terminal part of the spinal canal.

1.—*Lesions Developing on the Posterior Aspect of the Sacrum.*—

Suppuration occurs in a line with one of the spinal gutters. The symptoms are distinct and are those of an abscess in the tissues over the sacrum; the diagnosis is not difficult, and associated processes do not appear. Liquefaction may not occur until a week or more has passed. When the abscess is opened denuded bone is usually detected at the bottom.

2.—*Lesions Developing in the Parts of the Sacrum Bordering the*

Terminal Part of the Spinal Canal.—These lesions are apt to cause exudates in the interior of the spinal canal, which vary from extradural solid exudates to extradural abscesses and occasionally to intradural infections, that is, to spinal forms of meningitis. With the former the local neurologic symptoms assume the characteristics of syndromes usually associated with pathologic conditions of the sacral and coccygeal nerves (that is, the cauda equina syndrome). In cases of meningitis the meningeal symptoms dominate the picture.

3.—*Lesions in the Sacrum Situated Anteriorly.*—These lesions produce subperiosteal abscesses on the anterior surface of the hollow of the sacrum. They spread laterally and downward toward the inferior aperture of the pelvic girdle and are more or less easily palpable by rectum. The following paths can be distinguished anatomically:

(a) One form of lesion develops from the lower segment of the sacrum or from the coccyx. Suppuration from this source gathers in the interval between the coccyx and the anus and lies beneath the levator ani muscle and the anal fascia. Occasionally the pus spreads out of the pelvic cavity through the sacrosclatic notch and is discovered in the depths of the gluteal muscles; more commonly the pus courses downward and appears clinically as a para-anal or pararectal abscess.

(b) Another type of lesion develops above the line of attachment of the levator ani muscle. In the larger number of such lesions a subperiosteal abscess develops on the inner aspect of the bone between the bone and the iliacus muscle and spreads upward to the crest of the ilium, where it appears as an extraperitoneal abscess. In some cases the abscess points above Poupart's ligament. In a lesser number of cases an abscess forms which spreads forward and downward in the hollow of the sacrum and between the bone and the obturator and recto-

vesical layers of the pelvic fascia. The pus gathers in the ischiorectal fossa and appears clinically as a high ischiorectal abscess. In some cases an abscess spreads upward, so that it cannot be palpated from below through the rectal and or the vaginal canal or is palpable with great difficulty. This is the type of abscess which most frequently appears clinically as an obscure form of general infection (pyemia or sepsis).

In all the pelvic varieties of abscess the entire abscess lies within the pelvis. It is of the utmost importance to remember that the abscess is palpable by either rectal or vaginal examination or both. The ability to obtain the maximum amount of information by pelvic examination must be developed in order to treat lesions of this type.

For purposes of treatment the abscesses can be grouped as (*a*) high pelvic abscesses, (*b*) ischiorectal abscesses and (*c*) para-anal abscesses. The last mentioned are the simplest. Ischiorectal abscesses should be allowed to come down as far as possible; their proper incision is then much simplified. High pelvic abscesses are difficult to incise. In a certain number resection of the coccyx and possibly of the lowermost part of the sacrum is necessary in order to secure adequate drainage. The difficult ones are those which pass out of the pelvic cavity and point in a superficial location, as do some of the gluteal abscesses. The rule is to suspect an intrapelvic origin for any gluteal abscess in which there is retention of pus and which shows any tendency to retarded healing.

III. OSTEOMYELITIS INVOLVING THE FLARE OF THE ILIUM

Osteomyelitis of the flare of the ilium may point externally, in which case the pathologic condition is found principally in the tissues covering the external side of the bone. All the usual symptoms, of pain, tenderness and disability, are present; swelling is proportionate to the extent of the process and to the size of the subperiosteal abscess which forms under cover of the gluteal muscles. When the process is demarcated toward the internal visceral aspect of the bone the symptoms are referred to the loin, to the lower part of the abdomen and to the pelvis. Subperiosteal abscesses form under cover of the iliacus muscle and the tendon of the psoas muscle. Progression of the abscess may be upward, in which case the abscess points above the crest of the ilium or, in some cases, in a downward direction, toward the pelvic cavity. In the latter event the abscess is much more difficult to feel by rectum than are similar abscesses derived from the anterior surface of the sacrum.

A common complication and sequel is a perforation through the thin expansion of the flare of the ilium. Frequently this forms an insurmountable obstacle to the healing of the lesion until proper surgical measures are applied.

IV. OSTEOMYELITIS INVOLVING THE CENTRAL ACETABULAR REGION OF THE INNOMINATE BONE

In some cases any one or all of the acetabular parts of the ilium, the pubis and the ischium are involved. The following varieties are observable clinically:

A. In the first type the process in the bone is determined by the vascular distribution (see section on blood supply) of the lesion on its external aspect. Almost from the beginning the process is intracapsular, the joint is involved in the suppuration and the clinical picture is dominated completely by the symptoms of the joint involvement, even when additional pathologic conditions are plentifully present external to the joint capsule (for example, suppuration and sequestration in the extracapsular portions of the bone close to the joint).

The general symptoms are apt to be most prominent in cases in which the condition is of only ordinary severity, even when no overpowering general infection is present. The temperature is high, often reaching 105 or 106 F., and is apt to be sustained at those levels. Chills may occur. The blood cultures are usually positive during this stage. All of this is due to the retention of pus within the joint under increasing tension. Should the pus perforate the joint capsule and thread its way externally, the phenomenon of rupture is usually accompanied by amelioration of the general symptoms. Thereafter the temperature is variable, ranging usually from 101 to 104 F.

The local symptoms during the period of acuteness are pain, deformity, muscle spasm, diffuse swelling and tenderness in the general region of the hip. In some cases the pain is referred along the thigh to the knee. Movement is limited in all directions by muscle spasm, and pain is felt on any movement, especially when the leg is extended.

In the absence of a distinct abscess swelling is usually a general tumescence of the tissues of the hip surrounding the joint. This may be very slight. When the swelling is visible externally, rupture of the capsule and a secondary external abscess should be suspected, and the condition should be located, when possible, with the aspirating needle.

Local tenderness is almost always present anteriorly over the hip and posteriorly over the joint just behind the trochanter. Pelvic tenderness over the pelvic aspect of the acetabulum is usually slight, and no deformity of the contour of the bone at this area is felt during the pelvic (rectal) examination unless the suppuration succeeds in perforating the bottom of the acetabulum and spreading out beneath the pelvic periosteum and the pelvic fascia and between them and the bone. Such swellings are usually of moderate size because they drain into the joint and externally therefrom: usually, because of this fact, they need no special intervention and are resolved without treatment.

When the condition is acute there is flexion deformity of the thigh to the extent of an angle of about 40 degrees. Extension of the thigh when the patient lies on his back is accompanied by a definite downward tilting of that side of the pelvis. In addition, the lower limb on the involved side is rotated outward, and the knee is slightly flexed, in order to give the greatest comfort by relaxing the tissue and ligaments about the hip joint.

In this type of osteomyelitis it is usually impossible to tell from the general and local symptoms in which of the three segments of the central acetabular region the greater part of the osteomyelitic focus lies. Roentgenologic evidence is necessary to make the localization accurate.

The chief difficulty in differential diagnosis lies in the practical impossibility of distinguishing whether the lesion present lies in some part of the innominate bone or in the head or neck of the femur, whether the lesion is extracapsular or intracapsular or whether it is entirely a lesion of the joint. In the early stages this differentiation is impossible for lack of roentgenologic evidence; as soon, however, as roentgen aid is available this difficulty disappears.

Acute inflammatory rheumatism in the hip joint has many clinical resemblances to osteomyelitis. However, it is apt to be a polyarticular condition. The detection of a valvular or pericardial complication, so commonly found with acute articular rheumatism as to make its presence of diagnostic value, is of no clinical help in this differentiation, since similar lesions occur as a consequence of the general infection which precedes and accompanies acute osteomyelitis.

B. In the second type of osteomyelitis of this region the entire process remains extracapsular and never involves the joint. The general symptoms are approximately the same; the local symptoms show resemblance to those of foci of the type previously described, but they are ameliorated sooner, after which one can detect that the motions of the hip are relatively free. External abscesses appear, according to the location of the osteomyelitic focus, in each of the segments bordering the acetabular area.

C. Acetabular osteomyelitis of the third type is due to the situation of the lesion in the vascular channels supplying the visceral pelvic aspect of the acetabular region. The general symptoms are usually not as marked and are relatively benign; external swelling is nonexistent; and the characteristic local finding is a swelling on the pelvic side of the bone easily palpable by rectum and/or by vagina and situated opposite the joint. The swelling is a subperiosteal exudate or abscess. It is ordinarily of moderate size; and it rarely, if ever, perforates the joint across the thickness of the bone into the interior of the acetabulum. The "exudate" type of lesion is usually resolved spontaneously. The suppurative type does one of two things: It spreads upward and appears

above Poupart's ligament, or it spreads downward and, if large enough, assumes the characteristics of an ischiorectal abscess.

The lesion is usually easily demonstrable roentgenologically as a swelling corresponding to the palpatory findings on the inner aspect of the bone opposite the acetabulum.

V. OSTEOMYELITIS OF THE PUBIS

Chronic osteomyelitis of the pubis is found more commonly than the acute form, the reason for failure to recognize the process in its acute stage being that most pubic osteomyelitis is of the extension type in which the symptoms of the acute stage are lost in the manifestations of the original lesion to which the pubic osteomyelitis is secondary. In a review of the literature up to 1934 Jentzer was able to find a total of 16 cases of chronic hematogenous osteomyelitis of the pubis, in only 1 of which the condition was primary.

The reports of Jentzer⁴ and of Iseu⁷ are the best available ones regarding osteomyelitis of the pubis. Other reports of lesser value are those of Painter,⁸ Chauvin,⁹ McWhorter,¹⁰ Klemm and Gayet.¹¹

Jentzer was able to gather reports of 16 cases of chronic osteomyelitis in the literature up to 1934 (André, 2 cases; Painter, 3; Chauvin, 1; Marion, 1; Legueu, 2; Maisonnnet, 2; McWhorter, 1; Söderlund, 1; Gayet, 2; Klemm, 1). His report discussed principally the vesical complications. He mentioned reports of cases of acute osteomyelitis reported by Lévi, Painter, Lagos Cjarcia and Armando, Ingelrans, Zaffagnini, and Cajaccini.

Iseu was able to find 25 cases of acute osteomyelitis, presumably of the hematogenous variety, also up to 1934. Undoubtedly these two series overlap. Iseu discussed all phases of the subject.

Painter reported 3 cases, in 1 of which the condition was due to the staphylococcus, and in 2 of which it was due to the streptococcus.

In McWhorter's case the pathologic condition began as pharyngitis and acute otitis and was followed by acute osteomyelitis of the clavicle, the tibia and the pubis.

Söderlund's report included 3 cases of hematogenous and 1 case of extensional osteomyelitis. He made the statement that the hematogenous condition is never associated with sinuses which communicate with the vaginal tract. The presence of the latter, in Söderlund's opinion, indi-

7. Iseu, G.: *Chir. d. org. di movimento* **19:1**, 1934.

8. Painter, C. F.: Osteomyelitis of the Innominate Bone: Reasons for Rarity of Location; Methods of Repair, Operative and Otherwise, *J. A. M. A.* **86:341** (Jan. 30) 1926.

9. Chauvin: *J. d'urol.* **26:548**, 1928.

10. McWhorter, G. L.: *Surg., Gynec. & Obst.* **49:205**, 1929.

11. Gayet, in discussion on Chauvin.⁹

cates the history of a difficult labor, a tear in the vaginal mucosa and an extension of infection from the vaginal mucosa to the bone.

Osteomyelitis of the pubis is likely to be one of several lesions in the same person. In most cases the course is subacute, and in many cases a latent infection is present which comes to light only because of the occurrence of some complicating factor (see section on vesical complications). There are repeated exacerbations of pain and disability, with swelling anteriorly over the body of the pubis, along the superior ramus or on the fold of the perineum, where it passes into the inner side of the thigh corresponding to the descending ramus of the pubis.

During any period of acute exacerbation the pain, disability and swelling become more prominent. Disability is due principally to muscle spasm. External tenderness is present over the involved part of the bone. Rectal examination and, in women, vaginal examination yield information concerning any manifestations which point toward the pelvic cavity.

Marked swelling is always due to an abscess. The swelling may be located externally or may be situated internally in the pelvic cavity, where it may be discovered only on rectal or vaginal examination. The swelling and induration of the tissues may be located anteriorly around the neck and anterior surface of the bladder between the latter and the posterior surface of the pubis and are felt above the pubis by pelvic examination.

In many cases the entire clinical picture, the manifestations of the illness and the end result, is directly produced by the local complications of the osteomyelitis.

A. *Abscess Formations.*—Abscess formations occur almost invariably. According to the situation of the osteolytic focus, the abscess may be situated in either sex: (a) between the bladder and the posterior surface of the body of the pubis and the ascending ramus, that is, in the space of Retzius; (b) externally over the anterior surface of the body and ascending ramus of the pubis, spreading under the skin of the lower part of the abdomen and of the anterior surface of the hip and thigh; (c) externally over the external surface of the descending ramus of the pubis, spreading down in the fold of the perineum and down along the inner side of the thigh. In addition, in the male patient an abscess originating from a focus on the posterior aspect of the descending ramus of the pubis may take the anatomic position of an ischiorectal abscess. An extension from an abscess in some neighboring situation may also appear in the ischiorectal fossa. In women, an abscess may form (a) from the inner margin of the descending ramus, spreading along the lateral wall of the vagina or (b) from the posterior aspect of the pubis and its descending ramus, spreading along the lateral wall of the vagina and extending up toward and into the rectovaginal septum and the ischiorectal fossas.

B. *Vesical Complications*.¹²—In many cases of osteomyelitis of the pubis, even in those without original or associated trauma, vesical symptoms and complications occur. The biologic development of the vesical complications is as follows:

(a) *Pyuria*: Pyuria occurs as a single objective symptom, and when persistent it should call attention to the possible development of the following clinical progression.

(b) *Perforation of the Bladder*: Reports in the literature of perforation of the bladder from abscesses associated with osteomyelitis of the pelvis are not common. De la Peña¹³ in 1931 was able to find only 5 cases and added 1 of his own. In a discussion of Chauvin's⁹ paper before the French Society of Urology in November 1928 Maissonnet mentioned 2 cases, Marion 1 and André 1 (referred to previously). All the cases except André's were observed during the World War and were associated with injury to the pubic bone. This brings the total up to 10 cases, according to Hepler and Eikenbary.¹⁴

From their observation of 4 cases of severe chronic osteomyelitis of the pelvis in children Hepler and Eikenbary stated the opinion that this complication is often imminent in cases of suppurative lesions of the pelvic bones. This statement is based on the finding in all 4 of their cases of a definite displacement of the bladder and in 2 of the cases of perforation of the bladder by sequestrums with the formation of osteovesical fistulas. They assumed that perforation was impending in the other 2 cases because of the existence of the same engendering factors present in the 2 with perforation.

In the cases of Hepler and Eikenbary the displacement of the bladder was caused by a massive involucrum and not by a pelvic abscess. In each of the 2 cases with perforation the sequestrum plugged the opening of the osteovesical fistula. In 1 the opening was in the lateral aspect of the basal zone, and in the other it was in the fundal zone. In both the side of the bladder involved was firmly adherent to the involucrum, with a large amount of fungoid or granulomatous tissue between the bones and the bladder. The bladder wall at the point of perforation was so firmly adherent to the involucrum that there was no extravasation or urinary leakage. Nor was there any evidence of the previous existence of the conditions.

(c) *Vesical Fistula*: Under such conditions the further development of the complication leads to the formation of the osteovesical

12. It is most convenient to discuss the subject of vesical complications of osteomyelitis of the pubis here without regard to the type or character of the osteomyelitis or its originating or associated causative factors.

13. de la Peña, A.: *J. Urol.* **26**:473, 1931.

14. Hepler, A. B., and Eikenbary, C. F.: *Am. J. Surg.* **22**:113, 1933.

fistula. A fistula commonly extends from the bladder to the focal area in the bone or to the skin or communicates with the vagina or the rectum.

(d) Vesical Calculi: The next step is usually the formation of calculi, and, as in some of the reported cases, sequestrums are found to form the nuclei of the bladder stones. The calculi are apt to reform continuously until the vesical fistulas are closed and the osseous lesion is in a healing stage or is solidly healed.

In Marion's case the condition followed a bullet wound in the pubic region. There were no symptoms for two years; then there were marked vesical symptoms. Cystotomy was done, and a calculus was found. In the middle of the calculus a sequestrum was discovered. There was a recurrence of symptoms ten months later, when osteomyelitis of the pubis was demonstrated roentgenologically. A second calculus was found in the bladder and was removed. Permanent healing occurred thereafter.

Legueu¹⁵ observed 2 cases of war wounds with vesical symptoms and vesical fistulas. There was recurrent calculus formation. Healing of the fistulas took place after curettage of the sinuses and the bone. Nevertheless, there were many subsequent recurrences of the bladder stones.

Clinical Progression.—In some of the reported cases (Hepler and Eikenbary¹⁴) there were no subjective signs of vesical complication. This accounts for the failure to consider the possibility of this complication. Even in cases in which perforation is present, there may be no subjective symptoms. In a good many cases persistent pyuria was the first indication of the vesical complication.

In the others, the symptoms in the beginning are those of irritation of the bladder: frequent urination, pain, hematuria and pyuria. The vesical symptoms are commonly so prominent as to dominate the clinical picture and cause most of the symptoms. Under comparable conditions one should always think of the possibility of osteomyelitis of the pelvis (pubis), and one should not be misled by the apparent dominance of the urologic symptoms.

The presence of an apparently persistent fistula in the general neighborhood of the bladder should awaken similar suspicions and lead to similar investigations to prove or disprove the presence of osteomyelitis in the adjacent bone.

The same is true of the demonstration of vesical calculi. The repeated formation of stones should also point to the possibility of the presence of osteomyelitis.

Cystoscopic and roentgenologic examination should be employed as a routine in all these contingencies. When adequate information of this kind is available the diagnosis should not be difficult.

The operation for the cure of an osteovesical fistula is sometimes difficult because of the firm adhesions of the contiguous portion of the bladder to the involucrum and because of the infiltration about the

15. Legueu, F., in discussion on Chauvin.⁹

fistula; a frequent complication is more or less extensive laceration of the bladder. Healing is rapid, and the operative results are good. Once corrected, the condition does not tend to recur provided the osteomyelitis is adequately controlled.

VI. OSTEOMYELITIS OF THE ISCHIUM

Cases of osteomyelitis of the ischium fall into three groups:

1. Cases in which the condition is limited to the acetabular portion (body) of the ischium. These have already been described (see section on osteomyelitis of the acetabular portion of the innominate bone).

2. Cases in which osteomyelitis appears in the ascending ramus of the ischium. These are similar in all particulars to cases of osteomyelitis in the descending ramus of the pubis, and the differentiation can be made only roentgenologically. In some cases both the ischium and the pubis are involved, either simultaneously or consecutively by extension of the process. When the process is limited to the ischium, vesical complications are not likely to occur.

3. Cases in which there is osteomyelitis of the descending ramus and tuberosity of the ischium. It is almost impossible to differentiate clinically between these various areas except by roentgenologic means and by the facility with which foci in the descending rami spread into the body and then into the hip joint. According to McWhorter, the clinical picture and the roentgenologic evidences of this extension of the disease to the hip resemble very closely the picture of the type of acute nonsuppurative ankylosing arthritis described by Stern.

The general symptoms are similar to those in the cases in the other anatomically distinguished groups. The local symptoms are more or less similar also: pain, deformity, muscle spasm, swelling, limitation of motion and postural deformity. Tenderness is present over the involved part of the bone and is apt to be located medially and toward the posterior aspect. The physician has only the points of tenderness, the roentgenologic findings and the characteristic distribution of abscesses to enable him to attempt to make anatomic differentiations. As the ischium is situated medially and posteriorly to the hip and thigh, abscesses originating from the external, extrapelvic aspects of the bone are apt to be present on the posterior medial aspect of the thigh, beginning as collections of pus in the lowermost depths of the buttock and then spreading in a downward direction. Those which originate on the pelvic aspects of the ischium and point inward form the majority of the pelvic and ischiorectal abscesses which appear in association with osteomyelitis of the pelvic bones. For this reason rectal and vaginal examinations are important.

ROENTGENOLOGIC ASPECTS OF OSTEOMYELITIS OF THE PELVIC GIRDLE

In discussing the various phases of this subject many roentgenologic facts have been alluded to and described. These it is not necessary to repeat.

In the general consideration of roentgenologic facts relating to osseous tissue it must be remembered that lesions of the bone take a long time to develop sufficiently to produce differentiating shadows on the roentgenogram. When the periosteal layers are fully developed and can be clearly visualized in the pictures, the first signs of change are linear differentiations of the periosteum, which grow thicker as involucrem is deposited. As a general rule it takes from eight to ten days for these changes to become perceptible. The next changes occur in the osseous tissue and vary, in accordance with the length of time interposed from the beginning of the pathologic process, from smaller and larger areas of rarefaction to areas of necrosis and to completely differentiated and separated sequestrums of various sizes and shapes. In the thin plates of the iliums perforations are common. In the late stages the effects of destruction of osseous tissue are easily visible both in the amount of tissue destroyed and in the compensating morphologic changes of the remaining segments, as well as in the amount of involucrem which is formed. Comparison of the two sides of the pelvic girdle commonly give striking effects.

Tilting of the pelvis is evident in the roentgenograms. The shadows of the rami of the pubis and ischium overlap on the affected side, so that it is often necessary to retake the picture with the x-ray tube farther down in order to show the obturator foramen and the rami.

With proper technic in tilting the pelvis abscesses in the pelvic cavity can frequently be visualized in the films; and when the abscesses are beyond the reach of the finger the x-ray apparatus is an invaluable aid in demonstrating them.

In cases in which fistulas are present a roentgenogram taken after injection of the sinuses with a radiopaque solution will commonly indicate the origin of the suppuration.

The differential roentgenologic diagnosis is usually not difficult. Occasionally when the condition complicates a malignant lesion (see section on osteomyelitis following suprapubic cystotomy) care is necessary in distinguishing between the neoplastic and the inflammatory changes. The experienced roentgenologist should, however, have no difficulty in making the differentiation both under ordinary and under extraordinary conditions.

In all cases of suppurative lesions about the pelvis, of recurring lesions of this type about the pelvis or of similar lesions which do not heal after drainage, a causative focus in the bones of the pelvic girdle should be sought roentgenologically.

For emphasis, attention is again called to the relation of vesical calculi to sequestrums and inflammatory lesions about the bladder and the pubis, and to the importance of roentgenologic study as a means of ordinary and differential diagnosis (see section on vesical complications of osteomyelitis of the pubis).

TREATMENT OF OSTEOMYELITIS OF THE BONES OF THE PELVIC GIRDLE

Throughout this communication the general principles governing the treatment of the lesions have been indicated. It will be readily seen and appreciated that the treatment of osteomyelitis falls into two categories:

1. In treating osteomyelitis of the first type the physician is compelled by the anatomic situation of the lesion, by difficulties in diagnosis or by other equally important factors to assume a conservative attitude, and operation, even the simple incision of a frank abscess, must necessarily be done at an advanced stage of development of the lesion. Curiously, clinically it is found that the mortality either is not materially different or is less than when the condition is treated surgically.

2. For osteomyelitis of the second type surgical treatment of some kind is given. An analysis of these forms of treatment follows:

- (a) Simple incision and drainage of abscesses are done.

- (b) Unaided casting off of sequestrums is observed during the course of healing of the resulting sinuses; or occasionally this is aided by operative means.

- (c) In certain situations and under exceptionally favorable conditions osteotomies of various kinds are done. In the ilium these are usually more successful than in other locations, because the anatomic conditions are favorable.

- (d) Complications arise, such as vesical complications or occasionally spinal complications, which necessitate surgical treatment because of themselves rather than because of the osseous infection. Final success is always directly proportionate to the extent to which the bone lesion is susceptible to proper eradication and drainage.

- (e) Because of any or all of these reasons, sinuses and fistulas constantly develop, persist and show little evidence of permanent closure, and "revisions" of the apparent condition are constantly repeated. For this reason a belief in the hopelessness of any surgical intervention for these seemingly intractable lesions has become rooted among physicians.

It becomes apparent that except when complications (such as bladder complications) compel surgical therapy, the entire field of endeavor has consisted and still consists in incision and drainage of abscesses and repeated revisions of the resulting sinuses.

Abscesses superficial to the pelvic bones are usually under observation as they develop. Abscesses representing exceptions to this rule exist in association with the ischium, which is buried in the depths of the musculature. All other abscesses fail to come under observation until they are relatively old. The surgical approach to the latter abscesses is usually difficult or dangerous or both, and for this reason drainage is usually accomplished where the abscess finds its way to the skin and points. A persistent sinus usually follows. In the treatment of an abscess of the pubis and the ischium an approach through the medial side of the thigh is recommended by McWhorter: The adductor muscles are split, and a large area is opened, which permits drainage of practically all parts of the pubis and the ischium.

Sufficiently radical surgical treatment is possible only in the flare of the ilium. The technical procedure is simple. The bone is exposed and bared on each side at the site of the lesion by and through an appropriately placed incision. It is possible to resect the entire area of the lesion. Adequate drainage of any subperiosteal abscess should be provided. Frequently it is possible to do a secondary suture of the wound with a consequent material shortening of the period of invalidism.

In all other parts of the pelvic girdle radical operation has been considered difficult, not wise because of anatomic and physiologic difficulties or too dangerous to life; and not many surgeons have been sufficiently courageous to overcome these obstacles repeatedly. It must be confessed that this attitude is a wholesome one and is to be encouraged, as the practical aspects of the problem fit in with the best theoretic considerations regarding the correct and most advantageous method of treatment for osteomyelitis and refraining from intervention is the best that one can do at the present time in most of the cases.

The situation as regards therapy is best illustrated by the possibilities present in the treatment of lesions about the sacroiliac region.

Up to the time of Kulowski's report the treatment of osteomyelitis of the sacroiliac region was insufficient and unsuccessful. Surgeons have always considered suppurative lesions of this type originating in this region to be chronic conditions which are difficult and frequently impossible to heal. As a rule, drainage of the complicating intrapelvic or extrapelvic abscesses which usually occur has been the only treatment; and this treatment was recognized as being purely palliative. In hospital practice it was (and still is) not uncommon to have patients admitted for the incision and drainage of abscesses in the general sacroiliac region and then to have them readmitted periodically for revisions of the sinuses or for the incision and drainage of recurrent abscesses. No actual cure was ever obtained, and after a while such lesions were frequently thought to be extraordinary infections even when tubercle bacilli could not be found and other evidences of infection by specific organisms could not be proved.

It seems strange that surgeons did not attribute their uniform failure in the treatment of such a lesion to erroneous conceptions of the essential character of the process and to the insufficiency of their operations, although radical resection for tuberculosis was adequately described more than thirty years ago. The apparent neglect of similar treatment for the ordinary forms of osteomyelitis is understandable only because of the peculiar deep location of the lesions and the anatomic relations of the parts and because of the timidity of the surgeon toward operative attack in this region.

Bardenheuer ¹⁶ in 1899 was the first to urge radical resection of the sacroiliac joint for tuberculous involvement. The approach is made posteriorly through a modified Sprengle type of incision. The posterior half of the ilium is stripped subperiosteally on both the intrapelvic and the extrapelvic aspect, the sciatic notch being exposed. The ilium is sectioned vertically with a Gigli saw, which is passed through the lateral border of the greater sciatic notch. The mortality reported by Bardenheuer in 20 cases was 30 per cent. Schede since 1875 had done 26 such resections, with a mortality of 40 per cent and with 10 cures.

Painter ⁸ in 1908 reported 1 case in which the result of resection was fatal. The patient was in a desperate condition owing to tuberculous involvement of the entire region, and the operation was attempted as a last resort. Nevertheless, this apparently discouraged the further development of the procedure in this country.

Picque ¹⁷ in 1909 discussed total and partial sacroiliac resection for tuberculous osteomyelitis of the sacroiliac joint. His technic is a modification of that of Bardenheuer.

Kulowski's paper seems to be the first report of cases in which radical operations of this type have been deliberately undertaken for the cure of this form of chronic osteomyelitis. It goes without saying that the patient must be able to withstand a surgical operation. Pre-operative general hygiene, blood transfusions and even preliminary drainage of the soft tissue are indicated when the patient is considered unfit to be operated on. Fluids containing dextrose and salt may be given subcutaneously with advantage preceding, during and after the operation. The general clinical situation, and not roentgenograms alone, should determine the immediate indication. Operations of this radical nature should not be done in the acute stage of the disease, and the management of the condition should be left as much as possible to nature, surgical intervention being the last resort.

Briefly, the technic of the operation of Bardenheuer as modified by Picque is as follows: The incision follows the line of origin of the

16. Bardenheuer, S., cited by Krecke: *Centralbl. f. Chir.* **26**:1329, 1899.

17. Picque: *Bull. et mém. Soc. de chir. de Paris* **35**:1107, 1909.

gluteus maximus muscle and is sufficiently large to give plenty of room for the manipulations. The ilium is bared, and the bone is stripped of its periosteum on both sides as far as the great sacrosciatic notch and as far as the superior and inferior posterior spines. The line of section of the iliac flare is determined by the extent of the disease, and the section is best made with a power saw or with a Gigli saw. In the radical operation the margin of the sciatic notch is removed. The flap of ilium so defined is levered out, and the sacrum is exposed. Removal of the diseased parts in the sacrum is done carefully with chisel, mallet and curet. When the débridement is complete the resultant wound is packed wide open, a generous dressing is provided and the entire pelvis is adequately immobilized in plaster. Healing occurs by granulation and is tedious. In suitable cases, however, an attempt may be made to hasten the cicatrization by secondary suture. When this is not possible, I agree with Kulowski that the wound is ideal for the Orr method of treatment. As a matter of fact, because of the situation and nature of the wound one is compelled to adopt this method.

During the course of the operation both external and pelvic abscesses will probably be encountered. Every pocket must be thoroughly and widely opened, and sufficient bone must be removed to make the final cavity regular in shape and mechanically healable. The danger of injuring the rectosigmoid is remote, and injury to the pelvic portion of the ureter is perhaps more likely; both of these possibilities should be kept in mind. If the sacral canal is opened or if the débridement encroaches on the sacral foramens the danger of destruction of the sacral nerves is imminent. Fortunately, loss of function of any of these nerves is not nearly as serious as is destruction of the spinal nerves higher up.

The danger of uncontrollable hemorrhage is constantly present. Care must be taken at the sciatic notch to avoid injury to the superior gluteal artery and vein; several fatalities have been reported from this cause. Bleeding from the bone and from numerous small vessels in the soft parts is frequently troublesome. Shock is also a factor to be reckoned with because of the extent of the operation and is usually present in proportion to the amount of blood lost. Intravenous infusions of dextrose solution and transfusions of blood are frequently needed to combat the loss of blood and the resultant shock and collapse.

The chief feature of the procedure is to adapt the amount of resection to the extent of destruction present. The operation is entirely clinical, and one works carefully from the surface to the depths until a healthy firm bed of bone remains. This is the ideal attainment even though the sacral canal is opened. Except when the operation is in experienced hands this will probably not be attained, principally because of the timidity of the operator. This defect, however, ought readily to be remediable.

The only contraindications to the total operation are present in young women who might bear children, in the very young and in general in patients whose physical condition is unfit to withstand any surgical treatment.

In addition, Smith-Petersen¹⁸ in 1917 stated that this resection was too radical in any case except one in which the condition is extensive. He described his own ingenious lateral approach to the sacroiliac joint, in which a window is chiseled into the joint through the ilium. However, the primary surgical objective of the removal of diseased tissue, adequate drainage and subsequent immobilization, is not as thoroughly attained in the Smith-Petersen operation as in the operation of Bardenheuer and Picque.

Kulowski⁶ recognized the validity of some of these criticisms and for this reason has modified his procedure in cases presenting these difficulties, performing an incomplete operation the essential feature of which is incomplete removal of the iliac flare. Essentially this means retention of the margin of the sciatic notch and a much less radical operation. In suitable cases one might do a partial primary operation and complete the procedure secondarily when the general condition of the patient and all other factors warrant it.

Visual and static deformity need not necessarily result from the complete operation. In Picque's 7 cases the ilium finally fused with the sacrum, as it did in 1 of the cases reported by Kulowski. The dense mass of soft tissue and the scar usually prevent any herniation.

In all cases immobilization of the pelvis is an important item in the treatment. In many cases the essential principles of the Orr method of treatment are followed to great advantage. This is true especially with lesions involving the sacroiliac region. The immobilization should always be adequate. For lesions surrounding the hip joint and in those involving the hip joint proper the treatment should include immobilization of the thigh either by plaster of paris or by weight extension and suspension. Care is to be taken that the final position of the limb is not disadvantageous.

MORTALITY

In the series reported by McWhorter, Raeschke, Doran and Brown and Lloyd there were 10 cases of osteomyelitis of the pelvic girdle, with 1 death—a mortality of 10 per cent. In the Mount Sinai series of 12 cases there were 2 fatalities—a mortality of approximately 16 per cent. The private patient to whom I referred also recovered. This indicates a general mortality of 12 per cent for all forms of osteomyelitis of the various bones of the skeleton.

18. Smith-Petersen, M. N.: *Am. J. Orthop. Surg.* 15:593, 1917.

STUDIES OF HEPATIC FUNCTION BY THE QUICK HIPPURIC ACID TEST

I. BILIARY AND HEPATIC DISEASE

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AND

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NEW ORLEANS

When Pierson, cited by Robertson and his associates,¹ said some years ago that perhaps the greatest good that had come out of the search for adequate tests of hepatic function was the awakening of interest in the state of the liver, he probably did not himself realize how important his statement was, even though he went on to say that in this regard most physicians "have been asleep in Zion and are in need of a great revival." On all sides today are signs, though in some quarters they are faint indeed, of the beginning of that revival. Just as the patient with deficiencies of the cardiac, renal and respiratory apparatus has long been considered a poor operative risk, so is the patient with hepatic deficiency or insufficiency coming to be considered an equally poor, if not a poorer, risk.

Our own interest in the problem was first aroused by our study of the "liver death" or "liver-kidney syndrome" occurring in operations on the biliary tract, to which for the last several years we have devoted considerable time and attention. In our search for some method of determining the type of case in which this catastrophe is likely to occur we came to realize two important things about the liver: that its surgical role is by no means confined to disease of the biliary tract and that at least part of the problem would be solved if some adequate test of its function could be discovered.

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The studies reported in the three papers in this series have been made under the direction of Dr. Urban Maes, Director of the Department of Surgery in the School of Medicine of Louisiana State University. The technical studies have been made by Ruth Mayne, B.S. in Med. Tech., R.T. Members of the staff of Louisiana State University in Charity Hospital cooperated with us, as well as members of the staffs of the Tulane University and Independent Units, who furnished us with many cases.

1. Robertson, W. E.; Swalm, W. A., and Konzelmann, F. W.: Functional Capacity of the Liver: Comparative Merits of Five Most Popular Tests, J. A. M. A. 99:2071 (Dec. 17) 1932.

FUNCTIONS OF THE LIVER

Much of the present knowledge concerning the liver is due to the extensive clinical and experimental studies of Mann and his co-workers² at the Mayo Clinic. This organ, as Mann pointed out, is the servant of the body, as opposed to the pituitary gland, which is its master. From fetal life until life ends, the liver is a "physiological drudge," which constantly responds, often at the expense of its own cellular constituents, to the demands and needs of the rest of the organism. It has the ability to carry on many functions greatly in excess of normal needs, and it maintains those functions with extreme stubbornness, even when there is left only a small amount of normal functioning tissue with which to carry on. Indeed, Mann added, perhaps one of the reasons why the liver is so generally ignored is because of the efficiency with which it does its work under such adverse conditions.

The exact functions of the liver are still a matter of debate, and there is a rather general tendency to attribute to it any metabolic process which cannot be proved to take place elsewhere in the body. Disregarding that tendency, however, we are able to list certain of its functions which are fairly well established, even if they are not fully understood. These include:

1. The metabolism of carbohydrates. This function is possessed to some degree by all muscular structures, but the liver is the great storehouse of glycogen.

2. The metabolism of proteins. This function is not shared to an appreciable degree by any other structure, and the conversion to urea of the amino acids formed from proteins in the process of digestion seems to take place almost entirely in the liver.

3. The metabolism of bile. The bone marrow and the spleen share this function, but again the liver is the important organ. In it the bile acids, chiefly glycocholic and taurocholic acids, which are essential in the digestion of fats, are secreted in the form of salts.

4. The coagulation of the blood. The knowledge of the exact mechanism of this process is still confused, but the modern tendency, as the important studies of Quick, Stanley-Brown and others³ have shown, is to attribute a large part of the task to the liver. At least indirect evidence of this function is furnished in cases of hepatic injury, in which the prothrombin in the blood plasma is diminished.

2. Mann, F. C.: *Hepatic Physiology and Pathology from the Surgical Viewpoint*, Minnesota Med. **19**:695, 1936; *Hepatic Function in Relation to Hepatic Pathology: Experimental Observations*, Ann. Int. Med. **8**:432, 1934.

3. Quick, A. J.; Stanley-Brown, M., and Bancroft, F. W.: *Study of the Coagulation Defect in Hemophilia and in Jaundice*, Am. J. M. Sc. **190**:501, 1935.

5. The detoxification of poisons, bacteria and other harmful substances. This special function, again, is apparently shared with no other structure to any similar degree.

6. The thermogenic function. Crile,⁴ who is chiefly responsible for the emphasis now placed on this function, has shown that the liver produces approximately a third of the heat of the entire organism and that the introduction of heat within the abdomen causes a synchronous rise in the temperature of the liver and the brain.

The power of regeneration, which is sometimes described as one of the functions of the liver, must be constantly borne in mind, for it explains much that on the surface is confusing and contradictory. The Mayo Clinic studies have demonstrated that even when as much as 80 per cent of the liver substance is removed complete regeneration of the excised area occurs in six to eight months. They have also demonstrated that a relatively small amount of normal tissue is necessary for normal function. This explains why tests of hepatic function may give negative results even in the presence of such conditions as hepatic malignant tumor and hepatic cirrhosis as long as they remain localized, or, more exactly, as long as they do not involve the entire hepatic structure. It also explains why the mere existence of jaundice or the mere enlargement of the liver noted in various pathologic states does not necessarily bring about the condition loosely termed "liver insufficiency."⁵

The concomitance of pathologic changes in the liver and disease of the biliary tract was first noted by Reimann⁶ in 1917 and by Graham,⁷ who adduced both clinical and experimental proof, in 1918. Their work has been repeatedly corroborated, Flint's⁸ studies being especially important. He was able to show two things: that even macroscopically normal livers frequently reveal microscopic damage under such circumstances, and also (a fact of which we shall make considerable use in a later paper) that hepatitis is a rather frequent finding in nonbiliary disease even though no hepatic damage has been suspected.

4. Crile, G. W.: Function of the Liver in Relation to Operation on Gall-bladder and Ducts, *J. A. M. A.* **87**:309 (July 31) 1926.

5. Helwig, F., and Schutz, C. B.: A Liver Kidney Syndrome, *Surg., Gynec. & Obst.* **55**:570, 1932. Boyce, F. F., and McFetridge, E. M.: So-Called "Liver Death": A Clinical and Experimental Study, *Arch. Surg.* **31**:105 (July) 1935; "Liver Deaths" in Surgery: An Analysis of Thirty-Four Cases, *New Orleans M. & S. J.* **88**:563, 1936; The So-Called "Liver Death": An Experimental Study of Changes in the Biliary Ducts Following Decompression of the Obstructed Biliary Tree, *Arch. Surg.* **32**:1080 (June) 1936.

6. Reimann, S. P.: Cholesterol Content of Blood in Gallstone Disease, *Surg., Gynec. & Obst.* **26**:282, 1918.

7. Graham, E. A.; Cole, W. H.; Copher, G. H., and Moore, S.: Diseases of the Gall-Bladder and Bile Ducts, Philadelphia, Lea & Febiger, 1928.

8. Flint, E. R.: Association Between Gall-Bladder Lesions and Hepatitis in Human Subjects, *Brit. M. J.* **1**:1041, 1930.

Judd⁹ has suggested that the hepatitis which is often found at operation and which has given rise to no clinical manifestations may furnish, per se, actual evidence of the detoxifying activity of the liver. Bacteria, he noted, are only rarely demonstrated in such livers, but the gross findings are characteristic. The liver is enlarged; the tissue is firmer than normal; and the surface reveals many whitish lines. The edge of the liver may terminate sharply in such a whitish line or may be rounded and edematous. Heyd¹⁰ joined Judd in stressing the importance of routine inspection or palpation of the liver at all operations. He concluded that persons with small and atrophic livers are likely to respond poorly to surgical treatment, the response being in some way proportionate to the reduced size of the liver, and that such persons should be protected against possible postoperative hepatic complications before these have a chance to develop.

TESTS OF HEPATIC FUNCTION

At the present time most tests of hepatic function are highly unsatisfactory until the disease is so far advanced that the information which they supply is no longer necessary. They are of the same degree of crudeness, Graham¹¹ stated, as Richard Bright's test of renal function, which was performed by boiling urine over a spirit lamp. Certain things, however, may be said in their defense. In the first place, too much has been demanded of the individual test. Because of the wide variety of known hepatic functions, no one test can possibly be expected to reveal everything about the liver, and no single test should be relied on or condemned from so unreasonable a standpoint.

In the second place, no test of any sort takes the place of scientific knowledge, clinical experience and diagnostic acumen. Tests are of value only in proportion to the knowledge and wisdom of the physician who uses them. They may furnish additional facts, confirm a clinical diagnosis, less often establish it, indicate the risk of operation, suggest corrective preoperative therapy and point out the need of postoperative treatment, but more than this they cannot do, nor should more be expected of them. The chief and final responsibility remains the surgeon's.

In the third place, even repeated tests cannot be relied on implicitly, and a single test, we are inclined to say, should not be relied on at all. It is not inconceivable, as we have already implied, that the patient's

9. Judd, E. S.: *Physiology of the Liver and Its Relation to Surgery of the Biliary Tract*, *Ann. Surg.* **90**:1035, 1929.

10. Heyd, C. G.: *The Chemical Mechanism of Liver Protection in Abdominal Surgery*, *Tr. Am. A. Obst.* **46**:102-107, 1933.

11. Graham, E. A.: *Estimating the Risk of Operations on the Biliary Tract by Testing the Excretory Function of the Liver*, *Radiology* **21**:191, 1933.

state may be extremely grave while his hepatic function remains within normal limits as one is able to measure those limits. In other words, the most accurate of tests must be permitted a reasonable margin of error, and it is possible, because of the enormous reserve capacity of the liver, for a number of things to be seriously wrong while hepatic function remains unimpaired, at least by available standards of measurement.

Finally, it is impossible to employ the theoretically excellent precaution of performing every test on every patient, particularly when the tests involve (as so many of them do) repeated venous punctures. Quite aside from the time and expense inherent in such a plan, the average patient, as Robertson said, has decided objections to "being his own guinea pig." Even if he would tolerate it, there is a more fundamental objection. The type of patient who is most likely to be benefited by the information derived from multiple tests is also the type of patient who should not be submitted to miscellaneous venous punctures. Valuable as the information thus obtained may prove to be, it is by no means as valuable as the preservation of intact veins for the introduction of fluids which later may save life.

Mann laid down certain other requirements for tests of hepatic function which involve the use of extraneous substances. Before such agents are employed, he said, two things must be clearly demonstrated: that the liver destroys all, or at least a major portion, of the substance chosen, and that the direct or indirect quantitation of the substance is possible after it has passed through the liver. He added, rather caustically, that the sponsors of most tests previously proposed have seldom troubled themselves to meet these specifications. He added another warning, that the outcome of any test is likely to vary according to whether it is performed on a glycogen-empty or on a glycogen-filled liver. Our own results with the Quick hippuric acid test of hepatic function have demonstrated the importance of this consideration. It is also demonstrated by the recent experimental work of C. S. Stone (cited by Lehman¹²), on which we shall comment later, and by the work of Forsgen and Gerritzen,¹³ which suggested a definite rhythm in hepatic function.

Before proceeding to a consideration of the Quick test it is necessary to discuss the various tests of liver function which have previously been proposed. Such tests may be roughly classified under the headings of the various functions of the liver which they are supposed to illuminate,

12. Lehman, E. P., in discussion on Payne, R. L.: Postoperative Care in Surgery of the Bile Tract, *J. A. M. A.* **109**:1436 (Oct. 30) 1937.

13. Gerritzen, F.: Liver Diuresis as Result of Rhythmic Function of Liver, *Acta med. Scandinav.* **89**:101, 1936; abstracted, *J. A. M. A.* **107**:754 (Aug. 29) 1936.

aside from a large group of miscellaneous and often entirely illogical tests, most of which we shall ignore.

Tests of carbohydrate function include typically the galactose test¹⁴ and the levulose tolerance test. Both are based on the theory that in persons with hepatic dysfunction the rate of utilization of a predetermined amount of carbohydrate will be slower than in normal persons, and therefore a greater amount of the substance will persist in the general circulation and be excreted in the urine. The galactose tolerance test is generally regarded as unreliable. Jones,¹⁵ for instance, found its results normal in 2 cases of acute yellow atrophy, in both of which the diagnosis was proved by postmortem examination, and many other observers have had equally unsatisfactory results with it. Mann's conclusion was that too many factors are involved in the mechanism of sugar metabolism to make the test at all reliable, aside from the fact that there is a wide variation in the rate of utilization of dextrose by normal subjects.

The levulose tolerance test, while somewhat more accurate, is open to similar objections. Mann pointed out that the theory on which it is based is defective, in that the muscles as well as the liver make glycogen from levulose. His experiments performed in association with Bollman,¹⁶ furthermore, have demonstrated that a hepatectomized animal is capable of utilizing levulose. Flint, who found the test fairly accurate on the basis of a comparative histologic study of liver tissues, defended it on the ground that hepatic insufficiency can exist without clinical evidence; this defense, however, as we have pointed out, holds for all tests.

Studies on nitrogen partition have proved of no particular value, because extremely severe hepatic damage is apparently necessary to cause any significant alteration in these values. Studies of the urea, ammonia, amino acid, nonprotein nitrogen and uric acid contents of the blood have been made by competent observers, many of them by Mann and Bollman at the Mayo Clinic, with such varying and generally disappointing results that their independent value is practically nil. If they are employed at all, they should be considered purely of auxiliary value and should never be relied on for therapeutic or prognostic direction.

Tests of bile metabolism include typically the icteric index test, the van den Bergh test, the Fouchet test, the urobilinogen test, the test for bilirubinuria and the bilirubin test. The icteric index test is, as its name implies, a test for jaundice. It is a simple, reasonably accurate test, the

14. Jankelson, I. R., and Lerner, H. H.: Intravenous Galactose Liver Function Test, *Am. J. Digest. Dis. & Nutrition* 1:310, 1934.

15. Jones, C. M.: The Treatment of Acute Hepatic Insufficiency and Its Relation to Prognosis, *Am. J. Digest. Dis. & Nutrition* 3:624, 1936.

16. Bollman, J. L., and Mann, F. C.: Experimentally Produced Lesions of the Liver, *Ann. Int. Med.* 5:699, 1931.

chief value of which is in the revelation of latent or subclinical jaundice and in the demonstration of fluctuations in the icterus which cannot be detected by simple clinical observation. Its weakness lies in a consideration which we have already commented on, that the mere existence of jaundice does not necessarily imply a deficiency of hepatic function.

The van den Bergh test is a qualitative and quantitative estimate of the content of the bile pigment in the blood, based on the Ehrlich diazo reaction. It furnishes much the same information as does the simpler icteric index test, and it is open to such possibilities of misinterpretation that many observers are unwilling to use it at all as a test of liver function. The Fouchet test falls into the same category.

The urobilinogen test¹⁷ is based on the fact that urobilin produced in the intestinal tract is converted to bilirubin in the liver, completely if hepatic function is normal, incompletely if it is not (in which case it spills over into the urine as urobilinogen). Opinions vary widely as to the value of the test. Robertson stated that it merits little consideration. Elman and McMaster, as well as Pierson, in a discussion of Robertson's paper, stated that in their opinion it is the most delicate single test available for an estimate of liver dysfunction. It has the advantage of simplicity of performance, though there is disagreement as to how it should be interpreted. If no urobilinogen is present in the specimen it may be assumed that biliary obstruction is complete. If it is present in dilutions greater than 1 in 20, it may be assumed that hepatic damage is extensive. Killian in the discussion previously referred to pointed out that the rate of excretion varies at different periods of the day, as well as from day to day, in cases of catarrhal jaundice and allied conditions. In his opinion the test should be a twenty-four hour one, and the result should not be considered negative unless the negative reaction persists for five consecutive days. Five days, however, is a rather long period to wait for information about a seriously ill patient.

The presence of bilirubin in the urine as demonstrated by the bilirubinuria test is predicated on the presence of an excessive amount of bilirubin in the blood stream. The test is simple and is of undoubted value in conjunction with other tests. Few, however, would be inclined to be as positive as Leveruf and Berceanu (quoted by Graham), who stated that by its application the diagnosis of gallstone colic can be made within a few hours after the onset of symptoms and long before the appearance of jaundice.

17. Piersol, G. M., and Rothman, M. M.: Practical Value of Liver Function Tests, *J. A. M. A.* **91**:1768 (Dec. 8) 1928. Greene, C. H.; McVicar, C. S.; Rowntree, L. G., and Walters, W.: Diseases of the Liver: III. Comparative Study of Certain Tests for Hepatic Function in Patients with Obstructive Jaundice, *Arch. Int. Med.* **36**:418 (Sept.) 1925.

The bilirubin test of von Bergmann and Eilbott¹⁸ is undoubtedly a very sensitive test of hepatic function. Chemically pure bilirubin is introduced into the blood stream, and the amount in the plasma or serum is determined before the injection and also five minutes, three hours and four hours afterward, the amount recovered being interpreted as an index of the excretory function of the liver. The test has been greatly simplified since its introduction, but aside from the repeated venipunctures required the cost is prohibitive. Bilirubin costs approximately \$25 per gram, which makes a single test expensive and repeated tests, which we consider necessary in all cases, beyond reason for public charges and almost impossible for all but the most affluent of private patients. The test also has the serious defect that it cannot be used in cases in which jaundice is present. Harrop and Barron¹⁹ found that it frequently reveals unsuspected latent or subclinical jaundice; in their opinion, as in that of most observers, it is both accurate and delicate. Snell and Plunkett, on the other hand, were decidedly less enthusiastic.

Most excretory tests of hepatic function are based on the same principle, the injection of a dye into the blood stream and the determination of the degree of retention at stated periods thereafter. Various agents have been used for this purpose, but phentetiothalein sodium (phenoltetraiodophthalein sodium), which is now rather generally employed, is as satisfactory as any and, like the other halogen derivatives, has the additional advantage of making cholecystography possible at the same time.

The value of the dye test for hepatic function was discovered accidentally in Graham's²⁰ clinic, where its application has given brilliant results. In a study of 4 entirely unexpected "liver deaths" which occurred after operations on the biliary tract, it was found that all the patients had shown after cholecystography a high retention of dye, varying from 60 to 90 per cent. Later studies revealed that normal persons during the same period had a retention of only 10 to 15 per cent. The accidental finding was promptly turned to account, and since the method has been employed in Graham's clinic and no patient with a retention of more than 50 per cent of dye has been operated on without careful preparation, the mortality for cholecystectomy has been reduced from 6 per cent to 0.4 per cent and the mortality for operations on the common duct from 7.7 to 2 per cent.

18. Jankelson, I. R., and Gargill, S. L.: Bilirubin Liver Function Test: I. Modification of the Method, *New England J. Med.* 20:547, 1931.

19. Harrop, G. A., Jr., and Barron, E. S. G.: Excretion of Intravenously Injected Bilirubin as Test of Liver Function, *J. Clin. Investigation* 9:577, 1931.

20. Graham, E. A.: Lowering the Mortality After Operations on the Biliary Tract, *Illinois M. J.* 60:196, 1931.

Other observers have testified to the value of the dye test. Magath²¹ reported that it indicates obstruction long before the patient exhibits jaundice. Greene²² and his associates found it so constantly accurate in cases of portal cirrhosis that in the absence of positive findings they advised extreme caution in attributing ascites to a hepatic lesion. Greene also cited the finding of Chapman and his associates, that the average duration of life varies inversely with the degree of retention of dye. This would make the test valuable in determining the surgical risk versus the possible results of such operations for the relief of cirrhosis as the Talma-Morison omentopexy, splenectomy, and ligation of the coronary veins of the stomach. Greene and Conner²³ also considered the test valuable in determining the surgical risk of splenectomy and in demonstrating possible hepatic metastases from various types of malignant tumor. Bargen and his associates²⁴ have used it in this fashion in operations on the large bowel.

Lahey and his associates²⁵ have employed the test in several thousand cholecystectomies. They consider it very valuable but have warned against its use for patients with anginal and cardiac disease, emaciated patients, "poor risk" patients, jaundiced patients and patients with acute or subacute cholecystitis. For such subjects, Lahey stated, the introduction of the dye may cause an exacerbation of the disease which will require immediate operation. Obviously, these limitations materially reduce the usefulness of the test, for many such patients are included in the group of patients for whom information as to the state of hepatic function would be of extreme value.

The tests which we have mentioned are the principal tests of hepatic function in general use. Certain others less generally used must also be mentioned. Weiss²⁶ said that the lactic acid test is a useful prognostic aid in cases of jaundice, the elevation of the normal level (5.5 to 8.5) indicating a rapid destruction of glycogen in the liver and possible

21. Magath, T. B.: The Takata-Ara Test of Liver Function, *Am. J. Digest. Dis. & Nutrition* **2**:713, 1935.

22. Greene, C. H.; McVicar, C. S.; Snell, A. M., and Rowntree, L. G.: Diseases of the Liver: VI. Comparative Study of Certain Tests for Hepatic Function in Cases of Cirrhosis of the Liver, *Arch. Int. Med.* **40**:159 (Aug.) 1927.

23. Greene, C. H., and Conner, H. M.: Diseases of the Liver: V. Comparative Study of Tests for Hepatic Function in Certain Diseases of the Hematopoietic System, *Arch. Int. Med.* **38**:167 (Aug.) 1926.

24. Bargen, J. A., and Rankin, F. W.: Tests of Hepatic Function in Carcinoma: Their Value in Cases of Neoplasm of Colon With and Without Metastasis to Liver, *Ann. Surg.* **91**:225, 1930.

25. Lahey, F. H.: Present Management of Biliary Tract Disease, *S. Clin. North America* **12**:549, 1932. Clute, H. M.: Surgical Management of Obstructive Jaundice, *ibid.* **12**:565, 1932.

26. Weiss, S.: Liver Deaths and Their Prevention, *Am. J. Surg.* **23**:96, 1934.

impending toxemia. Epstein and Greenspan,²⁷ of Mount Sinai Hospital in New York, studied the cholesterol and the cholesterol ester content of the blood in cases of hepatic and biliary disease, finding the ester value markedly lowered in the presence of acute hepatic degeneration and inclined to be absent in cases in which the termination was rapidly fatal. The cholesterol values are less strikingly altered. In mild conditions the initial levels are only moderately depressed, and there is usually a prompt return to normal.

Determinations of serum albumin and globulin have been advocated by several authors. Foley and his associates²⁸ found that in the presence of advanced hepatic damage the albumin content of the serum is reduced and there is a reversal of the albumin-globulin ratio. Snell also found that both clinically and experimentally a rise in globulin and a fall in albumin indicate increasing hepatic damage, while the findings are reversed as improvement takes place. The Takata-Ara test, which was originally devised to differentiate meningitis from syphilitic involvement of the central nervous system, is also based on the ratio of albumin to globulin. It has the major defect, Magath pointed out, of being an empiric phenomenon and not yet explained on any satisfactory scientific basis. Its users report from 10 to 50 per cent of error, which is clearly too wide a margin for safety. Kirk,²⁹ who collected from the literature 3,583 cases in which it had been employed, concluded that its results are likely to be positive in any condition, hepatic or nonhepatic, in which the globulin level is elevated. Aside from its difficulty of performance, this makes it too insensitive to be used as a test of hepatic function.

Crandall, discussing the paper by Robertson and his associates to which we have referred several times, mentioned the test for blood lipase. Among 130 persons without hepatic disease he found only 6 with positive reactions for lipase, whereas the test yielded positive results in 80 per cent of patients with hepatic damage and in 100 per cent of experimental animals. It is not generally used.

Lichtman³⁰ in 1931 proposed a test for hepatic function based on the administration of a standard oral dose of cinchophen and a determination by colorimetric methods of the twenty-four hour excretion of oxycinchophen in the urine; excretion of more than 21 per cent of the

27. Epstein, E. Z., and Greenspan, E. B.: Clinical Significance of Cholesterol Partition of Blood Plasma in Hepatic and in Biliary Diseases, *Arch. Int. Med.* **58**:860 (Nov.) 1936.

28. Foley, E.; Keeton, R. W.; Kendrick, A. B., and Darling, D.: Alterations in Serum Proteins as an Index of Liver Failure, *Proc. Soc. Exper. Biol. & Med.* **33**:430, 1935.

29. Kirk, R. C.: The Takata-Ara Test and Its Relation to Cirrhosis of the Liver, *J. A. M. A.* **107**:1354 (Oct. 24) 1936.

30. Lichtman, S. S.: Cinchophen Oxidation Test of the Function of the Hepatic Cells, *Arch. Int. Med.* **48**:98 (July) 1931.

amount administered indicates hepatic dysfunction. The test seems to be very reliable. On the other hand, in view of Palmer, Woodall and Wang's³¹ comprehensive study of cinchophen and toxic necrosis of the liver one would hesitate to administer this agent, even in nontoxic doses, to patients in whom hepatic dysfunction was suspected, especially since the test, to be of value, demands repetition.

It is clear that most of the tests which we have outlined are unsatisfactory. The simpler tests are inaccurate or insensitive, if not both. The more reliable tests are too complicated for general use, or too expensive, or not applicable to the type of patient for whom they would be most useful. Finally, as we have already noted, the majority of such tests require repeated venous punctures, the information from which rarely compensates for the damage done to veins into which it may later be urgently necessary to introduce life-saving fluids.

QUICK HIPPURIC ACID TEST OF LIVER FUNCTION

In our own search for a simple, safe, reasonably accurate test of hepatic function, our attention was drawn to the hippuric acid test, advocated by Quick³² in 1932 and 1933. We have used it with increasing satisfaction for eighteen months, and have found that it possesses most of the advantages and is free from most of the disadvantages of the tests we have just listed. Before passing on to our own experiences with it, it may be of interest to outline the story of its development,³³ which is both curious and interesting.

The synthesis of hippuric acid was demonstrated by Wöhler in 1824. In 1877 Bunge and Schmeidenberg, in experiments long regarded as final, showed that hippuric acid was formed when the kidneys of dogs were perfused with benzoic acid and aminoacetic acid. They therefore concluded that the kidney was the site of the synthesis, and their observations were confirmed by Kochs in 1879 and by Cramer in 1902.

On the other hand, these experiments were not always accepted without question. In 1857 Kühne and Hallwachs had stated that the synthesis of hippuric acid might occur in the hepatic vessels in the presence of glycocholic acid. In 1911 Friedman and Tachau isolated hippuric acid after perfusing the liver of a rabbit with blood containing benzoic acid but no aminoacetic acid; they concluded that in this species

31. Palmer, W. L.; Woodall, P. S., and Wang, K. C.: Cinchophen and Toxic Necrosis of Liver: Survey of Problem, *Tr. A. Am. Physicians* **51**:381, 1936.

32. Quick, A. J.: Conjugation of Benzoic Acid with Glycine, a Test of Liver Function, *Proc. Soc. Exper. Biol. & Med.* **29**:12, 1932; The Synthesis of Hippuric Acid, *Am. J. M. Sc.* **185**:630, 1933.

33. Hirscheimer, A.: Synthesis and Excretion of Hippuric Acid in Pregnancy, *Am. J. Obst. & Gynec.* **29**:395, 1935.

the synthesis might occur in the liver. In 1915 Kingsbury and Bell³⁴ found hippuric acid in relatively large amounts in the liver after injections of aminoacetic acid and sodium benzoate; they suggested in their turn that the kidney was not the only organ in which the synthesis might occur. In 1918 Lackner, Levinson and Morse³⁵ poisoned dogs with hydrazine sulfate, which is known to affect only the liver and to leave the kidney intact, and found the synthesis of hippuric acid greatly diminished after the hepatic damage had been established. They considered their findings entirely in line with what is known of the characteristic synthetic function of the liver as compared with that of the kidney. In 1921 Delprat and Whipple,³⁶ experimenting with necrosis of the liver, caused by chloroform, also found that under these circumstances the synthesis of hippuric acid was much delayed.

In 1925 Bryan,³⁷ who was using the hippuric acid test as it had been used prior to that time, to determine renal function, found in 6 of 10 cases in which hepatic involvement was known to exist a constant and definite decrease in the excretion of the acid. At this time he advanced the hypothesis that the decrease might possibly be due to hepatic dysfunction, but until Quick's work was published there was still no suggestion that the method might be used for such a determination.

In 1932, in a study of the conjugation of benzoic acid in man, Quick found that the excretion of hippuric acid proceeded at a constant rate irrespective of the amount of sodium benzoate administered. He found, further, that the output of hippuric acid was greatly increased by the ingestion of aminoacetic acid or of foods rich in it. The conclusion seemed inevitable that the rate of formation of hippuric acid is dependent on the speed with which the organism can synthesize aminoacetic acid. Since it is established that the main site of the synthesis of aminoacetic acid is the liver, Quick reasoned that various degrees of hepatic damage would be likely to show a corresponding diminution in the excretion of hippuric acid and that the hippuric acid test, hitherto employed as a test of renal function, actually should be a more delicate test of hepatic function.

The logic of the reasoning is clear. The synthesis of hippuric acid is a process of detoxification which is brought about by the conjugation

34. Kingsbury, F. B., and Bell, E. T.: Synthesis of Hippuric Acid in Nephrectomized Dogs, *J. Biol. Chem.* **21**:297, 1915.

35. Lackner, E.; Levinson, A., and Morse, W.: Role of Liver in Hippuric Acid Synthesis, *Biochem. J.* **12**:184, 1918.

36. Delprat, G. D., and Whipple, G. H.: Studies of Liver Function: Benzoate Synthesis and Hippuric Acid Synthesis, *J. Biol. Chem.* **49**:229, 1921.

37. Bryan, A. W.: Clinical and Experimental Studies on Sodium Benzoate: Value of Sodium Benzoate Test of Renal Function, and Effect of Injury of Liver on Hippuric Acid Synthesis, *J. Clin. Investigation* **2**:1, 1925.

of benzoic acid and aminoacetic acid. The product of the conjugation is eliminated in the urine as hippuric acid except for a small fraction which is conjugated with glycuronic acid and eliminated as glycuronic acid monobenzoate. There is no store of preformed aminoacetic acid in the body; the liver has a maximum hourly synthesis of endogenous aminoacetic acid and in the absence of an exogenous supply cannot produce more than this maximum amount to combine with the ingested benzoic acid. The rate of synthesis of hippuric acid is therefore governed by the ability of the organism to produce aminoacetic acid. Since the liver is the site of the synthesis of this acid, it can reasonably be assumed that the synthesis will be adversely affected in the presence of certain types of hepatic damage and that the output of hippuric acid, which will be correspondingly diminished because of the lack of aminoacetic acid to combine with benzoic acid, will serve as an index of this damage.

The equations may be expressed as follows:

1. Sodium benzoate \rightarrow benzoic acid + aminoacetic acid \rightarrow hippuric acid.
2. Sodium benzoate \rightarrow benzoic acid + glycuronic acid \rightarrow glycuronic acid monobenzoate.

The author of the test, anticipating the objections likely to be raised to it, himself competently replied to them. The first possible objection is that the reserve of the liver is so great that impairment can be demonstrated only after extensive damage. This is true, Quick granted, in the sense that large portions can be removed surgically without lethal consequences, but proof exists that certain mechanisms are so delicate that there is practically no margin of safety. He adduced the experiments of Smyth and Whipple, which showed that a dose of chloroform too small to produce changes in the hepatic epithelium can cause a marked reduction in the excretion of the bile acids, and his own similar experiments, which produced a marked reduction in the output of glycuronic acid even when there were no histologic changes in the liver. The test indicates, he pointed out further, that the mechanism of the synthesis of aminoacetic acid seems to have no great margin of reserve, since the marked reduction in the excretion of hippuric acid in cases of catarrhal jaundice is out of all proportion to the characteristic structural changes in this type of pathologic condition.

The second possible objection is that the test indicates only one function of the liver. This is certainly true, Quick replied, but the hepatic functions are so intimately related to each other that injury to one mechanism may conceivably affect others. Thus the synthesis of amino acids, such as aminoacetic acid, depends on a precursor presumably derived from the metabolism of carbohydrates, while the forma-

tion of bile acids requires an ample supply of aminoacetic acid and taurine. The mechanism which synthesizes glycocholic acid is probably the same as that which effects the conjugation of benzoic acid and aminoacetic acid. Quick stated that it is significant that long-continued obstructive jaundice, which, as shown by Greene, Walters, Ravdin and others, brings about a decrease in the formation of bile acids, also brings about a reduction in the output of hippuric acid, neither substance returning to a normal level until a considerable time after the relief of the obstruction.

It is clear that the test is based on a normal physiologic process and for that reason involves no strain on the liver, such as is involved in almost all the other accurate tests for hepatic function, which require what we may describe as a superperformance. On the other hand, it would be foolish not to admit such valid objections as Mann's, that no conclusive proof yet exists that the liver is the sole site of the synthesis of hippuric acid. It would also be desirable, Mann added, to study the test in relation to the physiologic state of the liver at the time of its performance, as well as to have more information in regard to the rate of elimination of hippuric acid in the toxic nephroses, which are frequently associated with hepatic injury.

PRACTICAL CONSIDERATIONS IN THE USE OF THE QUICK TEST

The mention of renal disease brings to mind the precaution that the test should always be checked from that standpoint. Quick suggested a coincident determination of the nonprotein nitrogen content of the blood. We ourselves prefer, as did Kohlstaedt³⁸ and Helmer, the urea clearance test of Van Slyke.³⁹ We believe it more delicate, in view of Van Slyke's demonstration that as much as 20 per cent of renal damage can occur without alteration of the nonprotein nitrogen content of the blood. If renal damage is also present, the hippuric acid is retained as a nitrogenous product would be, and the test must be interpreted in the light of that fact. Snell, discussing the same subject, mentioned the work of Snapper and Grünbaum, who contended that there is some relation between the elimination of water and the elimination of hippuric acid. He suggested that erroneously low values may be obtained for patients who are dehydrated and who secrete only small amounts of urine, but this objection does not seem to us valid if the kidneys retain their power of concentration.

38. Kohlstaedt, K. G.: A Study of the Hippuric Acid Excretion as a Test of Hepatic Function, *Am. J. Digest. Dis. & Nutrition* 3:501, 1936.

39. Van Slyke, D. D., and others: Studies of Urea Excretion: Comparison of Blood Urea Clearance with Certain Other Measures of Renal Function, *J. Clin. Investigation* 8:357, 1930.

We have used the precipitation technic described by Quick and not the extraction method, which Kohlstaedt and Helmer considered more accurate in cases of jaundice; that has not been our experience. It is necessary, of course, that the specimens be stirred vigorously to precipitate the full amount of hippuric acid crystals; failure to observe this precaution is undoubtedly responsible for some inaccurate and misleading results. We also concentrate all specimens in which the crystallization is grossly small.

We formerly followed the exact technic described by Quick and collected and studied hourly specimens; for the last six months, after a series of careful comparative tests, we have been using a single four hour determination. We have found this method equally accurate and far simpler. It reduces the work in the laboratory and in the wards, which is a real consideration when nursing facilities are as limited as they frequently are in public hospitals. It also removes the objection, which is rather serious and frequent, that catheterization may be necessary to secure the hourly specimens at the appointed times; the risk thus introduced, especially when repeated tests are made, needs no comment. We have also found that the specimen can be stored in the ice box for hours or even for several days without affecting the accuracy of the test.

Sodium benzoate is nontoxic, and smaller doses are required for the test, Quick pointed out, than are administered therapeutically. It is inexpensive, which gives it an enormous advantage over the admittedly accurate bilirubin test. Hirscheimer has shown in his study of the use of this test for pregnant subjects that the drug can be administered intravenously, but we have not so employed it. He lists as possible sequelae diarrhea, anorexia and vomiting, as the result of local irritation of the gastrointestinal tract, and such symptoms referable to the central nervous system as headache, tinnitus, vertigo and reflex vomiting. Even with the repetition of the test, which is our custom, we have not seen such serious symptoms in any case.

In fact, the only case in our long series in which there was even a suggestion that the test had been dangerous is not particularly convincing. A Negro aged 66, with jaundice of undetermined duration, was operated on after a diagnosis of carcinoma of the pancreas had been made. Although he was an admittedly poor surgical risk, he had no special preparation except one infusion of dextrose. His preoperative hepatic function was 0.636. At operation the pancreas was demonstrably normal, and the symptoms were discovered to be due to a marked hepatic cirrhosis, for which cholecystostomy was done. The Quick test on the first day after operation was 0.435; one infusion of dextrose had been given. On the fourth day it was 0.437, and on the day before death, 0.257. Only one other infusion of dextrose had

been given during this period. One hour after each of the last two test doses had been administered the patient began to vomit, but there seems no doubt that by that time practically all of the sodium benzonate had passed out of the stomach. That the drug had a bad effect on the gastrointestinal tract of a seriously ill patient we are entirely willing to grant. That it had any part at all in the fatal outcome, as was suggested, seems unworthy of serious consideration; our own theory in this case, the only one in which such a question has arisen, is that a more liberal postoperative use of dextrose might have kept the patient alive for a longer period.

It must be granted, however, that we have been handicapped, at intervals, by the loss of the dose by vomiting, though for the most part this accident has occurred only in certain wards and then in epidemic waves strongly suggestive of a psychic or hysterical origin. The dose is usually retained if nurses and fellow patients refrain from helpful suggestions as to its nauseous effects. At one time we were obliged to discontinue the test for a period of weeks in a ward for white women because of the state of near-hysteria over it to which an excitable intern had reduced the patients, not one of whom was seriously ill and all of whom were being used for controls. In the wards for men and for Negroes it is unusual to have any trouble.

We have somewhat overcome the unpleasant taste of the sodium benzoate by the addition of a small amount of cherry syrup. Capsules are not practical. The required amount of the drug could not be put into fewer than six very large capsules, and the amount of water required to wash them down would probably alter the results of the test. We have wondered, in this connection, whether the slight dilatation of the stomach usually present after operation, as well as the alteration in absorption due to the physiologic alteration of the stomach under these circumstances, might influence the results, but the four hour period occupied by the test would seem to eliminate that possibility. We have had little trouble in giving the test even on the first day after operation, but we often withhold it because of the unwisdom of putting even small quantities of fluid into the stomach or because of the impossibility of forbidding the use of fluids for seriously ill patients for such a length of time.

We cannot say too emphatically that a single test does not furnish adequate information as to the state of the liver. Our own custom is to make the test on admission, after preparation for operation, and on the first, second, third, seventh and fourteenth days after operation, according to the length of the patient's stay in the hospital. We are willing to accept a single high or normal reading as correct if we are certain that there has been no unusual ingestion of carbohydrates, orally or otherwise, but we are unwilling to accept a single low reading as

correct, and we promptly repeat the test when such a result is noted. We check any possible loss of the sodium benzoate by vomiting or by failure to drink all of the solution; for several months we have made it our custom to have the receptacle in which the dose was given returned to us unwashed and still marked with the patient's name, so that we can check this point for ourselves. Also, to avoid possible errors in solubility, we use the patient's own urine to rinse out the beaker in which the precipitation is done, to be sure that the entire amount goes through the filter.

REPORTED RESULTS WITH THE QUICK TEST

Quick's first clinical report on this test included 36 cases, and his second,⁴⁰ 100 cases, some 80 of which were cases of hepatic or biliary disease. In the light of increasing experience he has seen no reason to alter his original opinion of the value of the test as an index of hepatic function and as a guide to diagnosis and prognosis. We agree with him that a low reading, particularly when it improves under correct preoperative preparation, does not necessarily indicate a fatal outcome, though we do regard it as a storm warning.

Vaccaro⁴¹ employed the Quick test in a group of 44 cases, in 27 of which the gallbladder and bile passages were involved. Twenty-six patients in the latter group of cases came to operation or autopsy, and there was a rather surprising accord between the results of the test and the operative and autopsy observations.

Snell and Plunkett⁴² used the test in a series of 38 cases of various types of jaundice. They said that it is a reasonably accurate and satisfactory index of parenchymatous hepatic damage, especially in the surgical types of jaundice. They noted little correlation between the results of this test and those of the galactose tolerance test but general agreement between the results and those of the serum bilirubin test. Our own idea is that if the Quick test and the bilirubin test could be used in combination for all patients they would furnish every reasonable safeguard from the hepatic standpoint, but the cost of the bilirubin test makes this plan impractical.

Kohlstaedt and Helmer used the Quick test in 77 cases, 41 of which were instances of disease of the liver and biliary tract. They reported a stormy postoperative course, and also some fatalities of the "liver death"

40. Quick, A. J.: Clinical Value of the Test for Hippuric Acid in Cases of Disease of the Liver, *Arch. Int. Med.* **57**:544 (March) 1936.

41. Vaccaro, P. E.: The Synthesis of Hippuric Acid, *Surg., Gynec. & Obst.* **61**:36, 1935.

42. Snell, A. M., and Plunkett, J. E.: The Hippuric Acid Test for Hepatic Function: Its Relation to Other Tests in General Use, *Am. J. Digest. Dis. & Nutrition* **2**:716, 1935.

variety, in patients with low readings. They stated that the test is reliable and of value for the detection of latent hepatic damage before clinical signs are evident.

Yardumian and Rosenthal⁴³ used the Quick test in 68 cases, 18 of which were instances of disease of the liver and biliary tract. They found the test reliable both independently and in comparison with other tests and reported it to be valuable in the differential diagnosis of hepatic and obstructive jaundice.

PERSONAL STUDIES WITH THE QUICK TEST

To date we have used this test in 82 cases of disease of the liver and biliary tract, of which the cases in which operation was performed are presented graphically (chart 1). Reducing the findings thus depicted

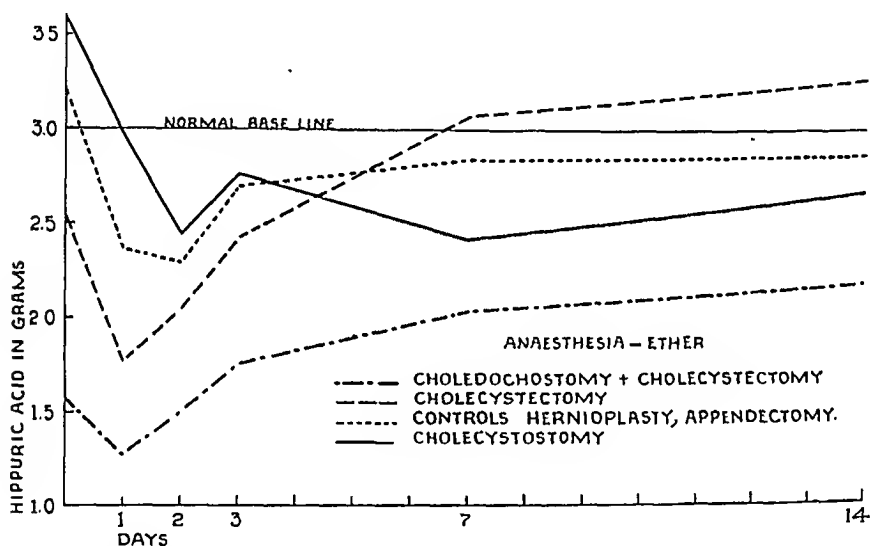


Chart 1.—Preoperative and postoperative results of the Quick hippuric acid test for hepatic function in cases in which operation was performed on the biliary tract.

to percentages of normal liver function gives the figures shown in table 1.

A study of these figures leads to some interesting and surprising conclusions. Highly significant in all cases, including those of the ether controls, which we shall discuss in detail in a later paper, is the marked impairment in hepatic function after operation. The drop on the first day is less marked after cholecystostomy than after other procedures, for obvious reasons. This operation is done on patients who are either very well prepared or respond very well to preparation. It involves less

43. Yardumian, K., and Rosenthal, P. J.: Hippuric Acid Elimination as a Test for Liver Function, *J. Lab. & Clin. Med.* 22:1046, 1937.

manipulation, time and trauma than do other biliary procedures. But the slow return to normal, even four weeks after operation, suggests the doubtful wisdom of prolonged drainage of the biliary tract and supports Judd's contention that there is rarely an occasion for cholecystostomy except as a temporary operation.

We are unprepared to make definite statements concerning the reason for the postoperative impairment of liver function. We doubt that any significant amount of hippuric acid is lost in the excreted bile. Perhaps infection is the cause. Perhaps the tube, which is a foreign body, sets up a reaction which spreads upward into the ducts. Probably the alteration of pressure in the biliary tree causes a loss of bile in the gastrointestinal tract, with a resulting decreased assimilation of fat. Since the metabolism of fat is related to the storage of carbohydrates, the glycogen in the liver is automatically diminished and the hepatic function correspondingly impaired. Whatever the reason, it might be well

TABLE 1.—*Percentages of Normal Hepatic Function*

Procedure	Preoperative		Postoperative (by Days)					
	1	2†	1	2	3	7	14	28
Cholecystectomy.....	77.5	51.7	60.0	71.2	90.2	96.0
Drainage of the common duct....	40.0	46.0	36.6	51.4	60.0	64.0	71.0
Cholecystostomy.....	77.2	107.7	87.0	72.0	82.0	71.0	78.0	81.0
Ether controls*.....	95.0	70.0	67.4	79.3	83.4	83.4

* Practically all biliary operations in this service are done with the patients under ether anesthesia.

† After preparation.

to bear in mind the effect of cholecystostomy on the liver, as shown by these tests, and to reflect that it may not be the simple and safe procedure it is usually assumed to be.

These figures show the importance of preoperative preparation and postoperative care in cases of biliary disease. The patients treated by means of cholecystostomy or operations on the common duct were all carefully prepared for operation, because, presumably, their state was more serious than that of patients on whom cholecystectomy was performed, most of whom appeared to be good risks. After all biliary operations it is our custom to give dextrose intensively for the first-day or two, and thereafter according to the indications. Except for the preliminary preparation and the postoperative bolstering of the liver by this therapy, the postoperative drop in function might have been far more marked and might have had far more serious consequences. As it is, the drop to 36.6 per cent of normal in the cases of operation on the common duct suggests the enormous reserve power of the liver, on which we have repeatedly commented, and its ability to carry on under the most adverse circumstances. Just how far that reserve

extends is a matter on which we are not at this time prepared even to speculate. The fall in hepatic function after cholecystostomy on the second day after the operation, when intensive dextrose therapy is usually discontinued except on special indications, is also striking. Our figures support the hypothesis that the degree of hepatic damage in terms of functional impairment is proportionate to the duration of the biliary disease (chart 2). When the obstruction had lasted for an average of two and two-tenths years the hepatic function averaged 2.626, 76.5 per cent of normal; when it had lasted for four and a half years the hepatic function averaged only 2.170, 63 per cent of normal.

The cases of toxic and catarrhal jaundice and those of miscellaneous hepatic conditions need no special comment (table 2). Unlike other observers, we found the values in cases of obstructive jaundice slightly

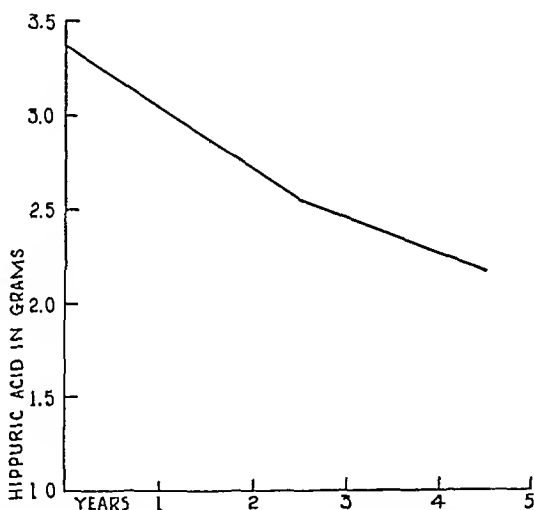


Chart 2.—Relation between the state of hepatic function and the duration of disease of the biliary tract, as shown by the Quick hippuric acid test.

lower than in cases of the toxic and catarrhal varieties, perhaps because of a possible longer duration in our cases. It is rather surprising, however, to find such low values with conditions of such relatively brief duration as are the toxic and catarrhal varieties of jaundice. We do not share Quick's opinion that the test is helpful in distinguishing between obstructive jaundice, in the presence of which the hippuric acid values are likely to be high, and toxic jaundice, in the presence of which they are markedly reduced, and should be unwilling to determine our therapeutic course on this basis. Snell and Plunkett shared our views.

We are inclined to lay no special stress on the relation between the icteric index and the values for the hippuric acid test of function. In cases of toxic hepatitis, in which the icteric index averaged 78, the hepatic function averaged 1.717, 50 per cent of normal. In cases of

TABLE 2.—*Typical Cases of Various Types of Jaundice and of Hepatic and Biliary Disease*

No.	Race	Sex	Age	Duration of Illness	Diagnosis	Quick Test	Comment
1	White	Male	61	4 months	Toxic hepatitis	0.692	Autopsy confirmation; icterus index 111
2	White	Female	18	?	Toxic hepatitis	1.462	Wassermann test + + + +; icterus index 83
3	White	Male	26	10 days	Toxic hepatitis	2.898	Prompt recovery
4	White	Female	23	5 weeks	Toxic hepatitis	2.937	Following treatment for malaria; test after recovery
5	White	Female	64	2 years	Toxic hepatitis	1.956	Acute attack 20 days previously; previous cholecystectomy; icterus index 67
6	White	Female	49	3 months	Toxic hepatitis	1.761	Icterus index 33
7	White	Female	21	1 week	Toxic hepatitis	1.307	Wassermann test + + + +; icterus index 250
8	White	Male	56	1 week ?	Catarrhal jaundice	0.726	Icterus index 250
9	White	Female	27	1 week	Catarrhal jaundice	0.758 0.905	Icterus index 200
10	White	Male	27	2 weeks	Catarrhal jaundice	3.382	Icterus index 166; test after intensive dextrose therapy
11	White	Female	16	2 weeks	Catarrhal jaundice	0.806	Wassermann test + + + +; icterus index 90.9; puerperal infection 6 months previously
12	Negro	Male	24	2 weeks	Obstructive jaundice	2.459	Wassermann test + + + +; icterus index 100; test after clinical recovery
13	Negro	Male	33	3 weeks	Obstructive jaundice	2.488	Icterus index 250
14	White	Female	60	25 years	Obstructive jaundice	1.526	Icterus index 56; common duct stone
15	White	Female	42	2 months	Obstructive jaundice	2.266	Acute cholecystitis; icterus index 23
16	White	Male	43	3 years	Hepatic cirrhosis	2.168	
17	White	Male	49	?	Hepatic cirrhosis	2.154	Admitted for scalp lesion; cirrhosis discovered in course of examination
18	White	Male	49	5 months	Biliary cirrhosis	1.061	Ascites; chronic alcoholism
19	White	Male	64	6 months	Biliary cirrhosis	0.715	Ascites; chronic alcoholism; repeated paracentesis; left hospital against advice, critically ill
20	Negro	Male	66	5 days	Biliary cirrhosis	0.636 0.435 0.437 0.259	Preoperative; one infusion 2d, 4th and 5th days after cholecystectomy, under ether; two infusions during this period; death 24 hours later
21	White	Female	31	6 months	Pyogenic abscess of liver	2.111 1.506	After repeated drainage
22	Negro	Male	29	10 weeks	Amebic abscess of liver	1.517	Died after 2d drainage

obstructive jaundice, in which the icteric index averaged 141, the hepatic function averaged 1.489, 43.2 per cent of normal. In cases of catarrhal jaundice, in which the icteric index averaged 140, approximately the same as in the obstructive type, the hepatic function averaged 1.697, 49.2 per cent of normal, practically the same as in the toxic type.

One or two illustrative cases may be mentioned. The most striking instance of failing hepatic function was furnished by a Negress aged 27, who had had epigastric distress for four months and jaundice for three weeks, associated with a considerable though undetermined loss of weight. She had a very large and tender liver. The icteric index was 67 on admission, and rose successively to 80 and then to 100. The urea content of the blood was 14.7 and the red blood cells 3,610,000. The Quick test reading was 0.5; we were just beginning to employ the test, and we did not appreciate the significance of this finding until later, when the patient died a typical "liver-kidney death" after cholecystostomy, which was done on a diagnosis of hepatic cirrhosis. The bile drainage became increasingly light and scanty, the urea content of the blood rose to 38, and for the last three days of life the patient was practically anuric, in spite of fluids given intensively by vein. Autopsy was not permitted, but the clinical syndrome was unmistakable. We tested this patient by the serum volume test for the hemorrhagic diathesis in jaundice, which we have just reported,⁴⁴ and, as we had predicted, there was no tendency to hemorrhage.

A white man aged 59, with a history of heartburn and painless jaundice for two weeks and no other symptoms of any sort, was also tested by the serum volume test. He showed an initial tendency to hemorrhage but none after preparation, and there was no bleeding at operation or afterward. The first Quick test gave a reading of 0.786, which by intensive preparation was raised to 1.859. This patient had had a cholecystostomy twenty years before, and at operation the anatomic distortion was so great that complete exploration of the common duct was impossible. Cholecystenterostomy was therefore done. He died in fifty-six hours, with typical hyperpyrexia; the temperature rose to 106 F. by axilla. Postmortem examination revealed no evidence of infection or hemorrhage, and the only positive finding was the hepatic necrosis which we have come to regard as typical of the so-called "liver death." Whether the hepatic damage as revealed by the first Quick test was too extensive to be overcome even by careful preparation we cannot say; the improvement in function as revealed by the second test may have been more apparent than real. Perhaps the patient's failure to respond to dextrose therapy as well as to decholin sodium (sodium dehydrocholate), with which we have had excellent results in

44. Boyce, F. F., and McFetridge, E. M.: A Serum Volume Test for the Hemorrhagic Diathesis in Jaundice, *J. Lab. & Clin. Med.* **23**:202, 1937.

some similar cases, was due to an inability of the liver to take care of the carbohydrates supplied. Kramer and his associates⁴⁵ have reported 2 such cases, in which the patients were children, and repeated blood sugar determinations might have settled this point.

Against these unfortunate cases may be set another. A 46 year old white woman told a rather indefinite story suggestive of a pathologic condition of the biliary tract of several years' duration. The icteric index was 200 at operation, and we regarded her as a frankly poor surgical risk, although the initial hepatic function of 0.671 had been raised by preparation to 1.708 and the serum volume test had revealed no tendency toward hemorrhage. Operation revealed an obstruction of the common hepatic duct, the type of which was not exactly determined; the duct was successfully drained after tedious dissection. Intensive dextrose therapy was continued for ten days after operation, and the convalescence was gratifying from every standpoint. The first postoperative Quick test, on the third day, showed a drop in the hepatic function to 1.219. Thereafter there was a small but steady rise, and when the patient was discharged, five weeks later, the reading was 2.283, more than three times as high as the initial reading. She has remained well to date, now eight months later. Why this patient, with a liver function on admission and after preparation slightly lower than those of the second patient described, should have gone on to uneventful recovery while the other patient lost his life is a problem for which we have no solution.

DEXTROSE THERAPY IN HEPATIC DYSFUNCTION

Our studies with the Quick test have made it clear that the premises on which dextrose has been used to bolster the liver are entirely sound. The clinical results of this mode of therapy are well known; the effect on the hepatic function of its use and withdrawal are shown by our figures, and research workers have had dramatic illustrations of what it can achieve. In recent (unpublished) work of our own on temperature reactions in hepatectomized dogs, we were able by this method to revive animals apparently at the point of dissolution eight and ten hours after operation. Their condition improved while the injection of dextrose was being made, and when it was finished they got to their feet and walked about the cage.

Althausen's⁴⁶ studies on dextrose therapy are very valuable. In one set of experiments he showed that insulin not only does not increase

45. Kramer, B.; Grayzel, H. G., and Solomon, C. I.: Chronic Hypoglycemia in Childhood, *J. Pediat.* 5:299, 1934.

46. Althausen, T. L.: Effects of the Administration of Glucose and Glycogen Content of Normal and Experimental Damaged Livers, *Ann. Int. Med.* 6:193, 1932; Dextrose Therapy in Diseases of the Liver, *J. A. M. A.* 100:1163 (April 15) 1933.

the hepatic glycogen but has precisely the opposite effect; his results suggest that the supposed beneficial effect of dextrose-insulin therapy is achieved by the dextrose in spite of the insulin. In another series of studies he was able to show the comparative effects of dextrose given by mouth and by vein. Biopsies of material taken at operation showed that patients who had received it intravenously for various periods had livers which showed moderate amounts of glycogen, while patients who had received it chiefly by mouth exhibited liver cells literally stuffed with glycogen. He suggested as a corollary to these findings that surgeons might remember the simpler method of oral administration before they resort to the more troublesome method of intravenous administration.

Jones⁴⁷ supplied further proof of the value of dextrose in cases of hepatic disease. In an analysis of 83 cases of hepatic insufficiency he found a 95 per cent mortality in the cases observed between 1922 and 1929, when dextrose was used in small quantities if at all, against a mortality of 63 per cent in the similar cases studied since that date, when dextrose therapy has been given as a matter of routine. In 1 case in our own series the patient has received so much benefit from the simple oral administration of carbohydrates that he has flatly declined the operation advised; his clinical improvement has been paralleled by the improvement in his hepatic function.

RELATION BETWEEN HEPATIC AND RENAL DYSFUNCTION

Jones brought up another matter which is mentioned by very few writers but which we ourselves think very important, the relation between hepatic function and urinary output. He went so far as to say that the prognosis in cases of hepatic disease can be based on the occurrence or failure of spontaneous diuresis, and he cited cases and statistics to prove his point. We have noted the same relationship in a large number of cases, some of them included in this series. Similar cases have been reported to us by other physicians who know of our interest in this matter.

An illustrative case might be mentioned. A white man aged 63, with a history of disease of the gallbladder for four years, had jaundice for the first time just before admission; there was no evidence of it clinically or otherwise after hospitalization. For many reasons he was regarded as a poor surgical risk, although routine tests, including the urea clearance test, gave normal values. The initial value for hepatic function was 0.847; after intensive preparation for ten days it was raised to 2.212. We might say at this point that we have no clear idea why

47. Jones, C. M.: *Newer Concepts of Liver Disease*, New England J. Med. **215**:432, 1936. Jones, C. M., and Eaton, F. B.: *Prognostic Significance of Spontaneous Diuresis in Acute or Subacute Disease of Liver*, *ibid.* **213**:907, 1935.

some patients respond to preparation so well and others so poorly. Cholecystectomy, choledochostomy and drainage were done. The gall-bladder and ducts were full of sand and a friable, necrotic material strongly suggestive of malignant tumor, although this diagnosis was later disproved in the laboratory.

The patient's immediate postoperative reaction was not good. He was listless and oliguric; the drainage of bile was scanty, and the prognosis was doubtful. The reading for the Quick test on the second day was 0.782. At this time we saw the patient in consultation and suggested the use of decholin sodium. Within four hours there was a free flow of bile, the patient had a large, spontaneous diuresis, and the entire clinical picture had changed; in particular, the distressing listlessness had entirely disappeared. The convalescence was stormy, being complicated by an infection of the upper respiratory tract and a partial wound rupture, but the tendency to recovery was clear. Injections of decholin sodium were given every eight hours for twenty-four hours. The value for hepatic function on the third day after the operation had risen to 1.749, and although it fluctuated and at no time rose above 2.289, it never again fell to a disturbingly low level. The patient has remained well from the standpoint of his biliary disease, although three months after his discharge he exhibited a malignant tumor of the larynx, from which at the time of writing he is slowly dying.

Many explanations have been advanced of the relation between hepatic and renal function. We are particularly impressed with that of Bruhl and of Watzadse, which Vaccaro quoted. They found in their experimental work on frogs that a lack of aminoacetic acid brought about a cessation of glomerular circulation. On this basis it seems not unreasonable to assume that the liver, by means of the amount of aminoacetic acid released into the circulating blood stream, actually determines renal function. If this is true, we are justified in interpreting the progressive oliguria, passing over into anuria, which is the outstanding characteristic of the "deferred liver death" or "liver-kidney" syndrome, as due to a diminished synthesis of aminoacetic acid in the liver.

We have heretofore explained this syndrome on the basis of the inability of the liver to take care of the products brought to it for detoxification and the resulting damage of the convoluted tubules of the kidney caused by the undetoxified products shunted on to the kidney by the failing liver. We did not accept the theory of Helwig and his co-workers, that these toxins have a special affinity for the kidney. We were never fully satisfied with our explanation, however, for we did not consider that the renal damage, as manifested by histologic study, was sufficient alone to account for the marked depression of renal function that is clinically apparent. It now seems to us more reasonable to assume that the impairment of the synthesis of aminoacetic

acid by the liver, as manifested by a decreased excretion of hippuric acid, is the basic deficiency. Certainly the improvement following the administration of decholin sodium, with, as has been proved, the resulting improvement first in the synthesis of aminoacetic acid and then in the formation of bile acids, would seem to support this view, entirely aside from the actual clinical results we have repeatedly witnessed after the use of this agent.

Whatever be the truth of this hypothesis, the important consideration is that a patient who exhibits a damaged hepatic function before operation, as manifested by a failure of synthesis of aminoacetic acid, becomes a doubly poor risk if there are also apparent signs of renal damage, such as a raised urea content in the blood and a low urea clearance.

SUMMARY

The increasingly important role of the liver in biliary surgery is pointed out.

The functions of the liver are outlined, and its capacities and reserve power are discussed.

The value and limitations of tests for hepatic function are considered.

The advantages and disadvantages of the tests in general use are outlined.

The development of the Quick hippuric acid test of liver function is sketched; its advantages and disadvantages are listed, and special phases of our experience with it are discussed.

The results of our personal experience with the test in cases of biliary and hepatic disease are set forth, and such special points are discussed as preoperative preparation, the postoperative drop in function, the relation of functional impairment to duration of illness and the extreme importance of dextrose therapy preoperatively and postoperatively. Illustrative cases are reported.

The close relation between hepatic and renal function is pointed out, and experimental and clinical proof of this relation is outlined. The generally good results following the use of decholin sodium are noted, and it is suggested that patients suffering from both hepatic and renal dysfunction should be regarded as dubious risks for operation.

NOTE.—Shortly after this paper was written, Dr. Quick supplied us with an intravenous test, a modification of his original test. This modification permits the use of the test immediately after operation and for seriously ill patients and therefore meets certain of the objections we have outlined. We have used the intravenous Quick test in approximately 50 cases of disease of the thyroid gland and biliary tract and have found it as satisfactory as the oral test.

STUDIES OF HEPATIC FUNCTION BY THE QUICK HIPPURIC ACID TEST

II. THYROID DISEASE

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AND

ELIZABETH M. McFETRIDGE, M.A.

NEW ORLEANS

In a previous communication¹ we have discussed in detail the rationale of the Quick hippuric acid test for hepatic function and have considered its reliability as an index of hepatic damage in cases of hepatic disease and of disease of the biliary tract. In this second communication we shall consider its value as an index of hepatic function in the presence of thyroid disease, for which purpose we have been employing it for the past eighteen months. Before discussing it from this aspect, however, it is necessary to consider the justification for any test of hepatic function under these circumstances, which means that we must trace the relation between the liver and the thyroid gland.

It is surprising to find how commonly that relation is ignored. The majority of writers list hyperthyroidism as the chief cause of death of toxic thyroid disease, but they make no attempt to explain the origin of the state called thyroid crisis. On the other hand, Dinsmore,² in the chairman's address before the Section on Surgery of the American Medical Association in 1937, made the unqualified statement that the most common cause of postoperative delirium and disorientation after operations on the thyroid gland is hepatic failure, and Lahey³ has repeatedly stated his belief that deaths associated with hyperthyroidism are chiefly "liver deaths." These physicians are authorities in the field of thyroid disease, and they know whereof they speak. We share their

From the Department of Surgery of the School of Medicine, Louisiana State University, and the Charity Hospital of Louisiana.

1. Boyce, F. F., and McFetridge, E. M.: Studies of Hepatic Function by the Quick Hippuric Acid Test: I. Biliary and Hepatic Disease, *Arch. Surg.*, this issue, p. 401. This contains an extensive list of references which are not repeated here.

2. Dinsmore, R. S.: Factors Influencing Morbidity in Thyroid Surgery, *J. A. M. A.* **109**:179-183 (July 17) 1937.

3. Lahey, F. H.: Reduction of Mortality in Hyperthyroidism, *New England J. Med.* **213**:475-479 (Sept.) 1935.

opinion. The sudden and extreme hyperpyrexia which may occur post-operatively and even preoperatively, the jaundice, which is sometimes slight and transient but more often deep and terminal, and the benefit produced in cases of thyroid disease by the measures ordinarily used to combat hepatic damage, all seem to establish the thesis.

We became interested in this aspect of thyroid disease in the course of our studies on the "hyperpyrexia death," or "liver death" which sometimes follows operation on the biliary tract. The same type of clinical picture, dominated by hyperpyrexia with a rapidly fatal outcome, has become classic in the literature on thyroid disease, under the terms postoperative crisis or thyroid storm, and the same type of microscopic hepatic damage noted after such deaths in cases of biliary disease can be noted after similar deaths from thyroid disease. The same clinical and pathologic picture is also seen in cases of untreated or mismanaged thyroid disease for which operation has not been done.

HISTORICAL DATA CONCERNING THE HEPATOTHYROID RELATION

The whole subject of hepatic changes in cases of toxic thyroid disease has recently been reviewed by Cameron and Karunaratne.⁴ As they pointed out, Paul in 1865 was the first to mention the association of hepatic cirrhosis and toxic thyroid disease. Three years later Trousseau again referred to the possible association. Jaundice was first mentioned by Habershon⁵ in 1874, and Burton⁶ in 1888 reported its transient occurrence in a male patient with exophthalmic goiter. White⁷ in 1886 had described the same disease as occurring in a woman aged 47, in whom autopsy revealed hepatic cirrhosis. In 1898 Sutcliff⁸ reported "an extraordinarily acute case of Graves' disease" in a female patient who exhibited exophthalmos, emaciation, a racing pulse, persistent vomiting and antemortem jaundice, the whole illness occupying only three months. Eder⁹ in 1906, in a report of 3 cases of jaundice in which the condition was associated with exophthalmic goiter, seems first to have realized the causal relationship, though his idea of the basis

4. Cameron, G. R., and Karunaratne, W. A. E.: Liver Changes in Exophthalmic Goitre, *J. Path. & Bact.* **41**:267-282 (Sept.) 1935.

5. Habershon, W.: Exophthalmic Goiter; Heart Disease; Jaundice; Death, *Lancet* **1**:510, 1874.

6. Burton, F. W.: Pigmentation and Other Cutaneous Affections in Graves' Disease, *Lancet* **2**:573, 1888.

7. White, W. H.: On the Prognosis of Secondary Symptoms and Conditions of Exophthalmic Goiter, *Brit. M. J.* **2**:151-153, 1886.

8. Sutcliff, E. H.: An Extraordinarily Acute Case of Graves' Disease, *Lancet* **1**:717, 1898.

9. Eder, M. D.: Three Cases of Jaundice Occurring in Persons Suffering from Exophthalmic Goiter, *Lancet* **1**:1758, 1906.

thereof, some toxemia of the intestinal canal "with the seat of action in the pituitary body," would need considerable editing today. This author noted that although jaundice was not mentioned in English texts as a possible accompaniment of toxic goiter, it had been referred to by Dieulafoy in his "Pathologie Interne" published in 1901.

Marine and Lenhart¹⁰ in 1911, in a study of the pathologic anatomic picture in the presence of exophthalmic goiter, noted a well marked generalized thickening of Glisson's capsule in 5 cases, in 4 of which atrophic cirrhosis was present. Such livers, they pointed out, tended to be reduced in volume, and the cells usually exhibited some degree of fatty metamorphosis. In 1919 Kohn¹¹ reported 56 cases of exophthalmic thyroid disease, in 5 of which jaundice was present, and a group of 43 miscellaneous cases, including instances of acute thyroïdism as well as of nontoxic disease, in 6 of which jaundice was present. In 1922 Kerr and Rusk¹² reported acute yellow atrophy of the liver following hyperthyroidism, with marked parenchymatous degeneration of both liver and kidneys, and in a later communication Kerr¹³ reported the observation of several similar cases.

Barker¹⁴ in 1930 described the interesting case of a white female patient admitted in coma, who died in twenty-four hours. Later a history of exophthalmic thyroid disease was secured; the condition had been treated with iodine. Postmortem examination revealed a small liver, with areas of necrosis and passive congestion, and tubular degeneration of the kidneys. He considered the hepatic condition analogous to the cardiac necrosis sometimes encountered in cases of exophthalmic goiter. Forbes¹⁵ by illustrative cases called attention in 1934 to the possible confusion, because of the similarity of the picture, between postoperative hepatic failure and a crisis of latent or potential thyroid disease, not previously suspected, after nonthyroid surgical treatment. He suggested that in all such cases compound solution of iodine U. S. P.

10. Marine, D., and Lenhart, C. H.: Pathological Anatomy of Exophthalmic Goiter, *Arch. Int. Med.* **8**:265-316 (Sept.) 1911.

11. Kohn, L. W.: Gastrointestinal Symptoms in Disturbances of Thyroid, *New York M. J.* **110**:1066-1068, 1919.

12. Kerr, W. J., and Rusk, G. Y.: Acute Yellow Atrophy Associated with Hyperthyroidism, *M. Clin. North America* **6**:445-459 (Sept.) 1922.

13. Kerr, W. J.: Necrosis of Heart and Liver in Thyrotoxicosis, with Some Notes on Possible Changes in Other Organs, *Northwest Med.* **29**:430-431 (Sept.) 1930.

14. Barker, L. F.: Thyro-Intoxication with Necrosis and Atrophy of the Liver, Damage to Heart Muscle and Kidneys, and Terminal Bronchopneumonia, *M. Clin. North America* **14**:261-263 (July) 1930.

15. Forbes, R. D.: Hyperthyroidism After Abdominal Operations, *S. Clin. North America* **14**:1339-1346 (Dec.) 1934.

be used as a tentative therapeutic measure. Parturier and Delerue¹⁶ in the same year stated that 30 per cent of patients with hepatic disease present signs attributable to the thyroid; they suggested the addition of liver therapy to the thyroid treatment. It was their idea that clinically the effect of the thyroid on the liver is less marked than the effect of the liver on the thyroid; "thyroid function is unlatched only when hepatic function fails." Their arguments, it seems to us, suffer from the rather general tendency to overemphasis which we have observed in most of the communications from the French school on the subject of hepatic disease.

On the experimental side, Farrant¹⁷ in 1913 showed that thyroid-fed cats and rabbits exhibited fatty degeneration of the liver, most marked around the center of the lobules and associated in some instances with changes suggestive of tubular nephritis. In 1917 and again in 1918 Kuriyama¹⁸ studied the effect of thyroid feeding on white rats. Within three to five days after the feeding was begun the animals all exhibited a decreased glycogen content of the liver, though control rats in which a similar loss of weight was produced by regulation of the diet showed no such depletion. Within two or three days after thyroid feeding was discontinued the hepatic glycogen returned to normal, even though the body weight was not regained. In 1921 Hashimoto¹⁹ and later Goodpasture²⁰ fed albino rats with thyroid substance in an endeavor to reproduce the myocardial changes noted clinically in hyperthyroid disease; this treatment produced not only those changes but also parenchymatous changes in the liver and in the convoluted tubules of the kidneys. Himmelberger,²¹ in 1932 by injecting into mice blood serum or urine from patients with exophthalmic goiter was able to demonstrate a substance capable of disturbing the glycogenic function of the liver, although no hepatic change was noted in 40 control animals which received the same sort of injections from patients without thyroid dis-

16. Parturier, G., and Delerue, J.: Les syndrômes hépato-thyroïdiens, *Rev. méd.-chir. d. mal. du foie* **9**:187-218 (May-June) 1934.

17. Farrant, R.: Hyperthyroidism: Its Experimental Reproduction in Animals, *Brit. M. J.* **2**:1363-1367, 1913.

18. Kuriyama, S.: Influence of Thyroid Feeding upon Carbohydrate Metabolism, *Am. J. Physiol.* **43**:481-496 (July) 1917; Influence of Thyroid Feeding upon Carbohydrate Metabolism: I. Storage and Mobilization of Liver Glycogen in Thyroid-Fed Animals, *J. Biol. Chem.* **33**:192-206 (Jan.) 1918.

19. Hashimoto, H.: Heart in Experimental Hyperthyroidism with Special Reference to Its Histology, *Endocrinology* **5**:579-606 (Sept.) 1921.

20. Goodpasture, E. W.: Myocardial Necrosis in Hyperthyroidism, *J. A. M. A.* **76**:1545-1551 (June 4) 1921; Influence of Thyroid Products on the Production of Myocardial Necrosis, *J. Exper. Med.* **34**:407-423 (Oct.) 1921.

21. Himmelberger, L. R.: Thyroid Hormone in Blood and Urine in Graves' Disease, *Endocrinology* **16**:264-266 (May-June) 1932.

ease. In 1935 Habán²² was able by thyroid feeding to produce necrotic changes in the livers of cats and rabbits, as well as a marked or complete depletion of the glycogen content; the changes were less marked in guinea pigs.

For the last three or four years the relation between the liver and the thyroid has been studied intensively in groups of cases rather than casually observed in single cases such as we have listed. Thus Weller²³ in 44 autopsies on patients with hyperthyroidism found the liver normal in only 6 cases; the hepatic involvement was moderate in 16 cases and marked in 22. In a control series exactly the reverse was noted; the liver was normal in 30 cases, moderately damaged in 13 and severely damaged in only 1. Rowe²⁴ in a study of 4,000 cases of various diseases found the incidence of hepatic damage, even including figures which he termed "heavily over-weighted," to be at most 10.9 per cent, whereas in 644 autopsies for hyperthyroidism he found the incidence of hepatic damage to be 22.44 per cent, more than twice as high.

Beaver and Pemberton²⁵ from the Mayo Clinic analyzed 107 autopsies for toxic thyroid disease, the study covering ten years and including both the iodine and the preiodine period. In 98 cases, 91.5 per cent of the total number, some hepatic involvement was noted. Acute hepatic lesions occurred in all patients who had died in crisis, as well as in 96.5 per cent of the patients whose basal metabolic rates were higher than + 60. Similar lesions were present in all patients with jaundice. The authors concluded that such lesions are an integral part of the syndrome of exophthalmic goiter and may be assumed to be due directly to thyroid intoxication, since they are usually proportionate in their degree to the intensity or the duration of the thyroid disease, or both. Ragins²⁶ has reported 6 such cases, and Cameron and Karunaratne have added 30 cases in which autopsy was performed at the University College Hospital Medical School, London, England. They also listed 30 cases reported by Rossle and 26 by Haban.

In studying the deaths from thyroid disease for the last ten years at the New Orleans Charity Hospital in the course of our investigations

22. Habán, G.: Leberveränderungen bei experimentellen Hyperthyreoidismus, Beitr. z. path. Anat. u. z. allg. Path. **95**:573-589, 1935.

23. Weller, V. V.: Hepatic Pathology in Exophthalmic Goiter, Ann. Int. Med. **7**:543-560 (Nov.) 1933.

24. Rowe, A. W.: Endocrine Studies: XXXV. Association of Hepatic Dysfunction with Thyroid Failure, Endocrinology **17**:1-22 (Jan.-Feb.) 1928.

25. Beaver, D. C., and Pemberton, J. deJ.: Pathologic Anatomy of Liver in Exophthalmic Goiter, Ann. Int. Med. **7**:687-708 (Dec.) 1933.

26. Ragins, A. B.: Value of Takata and Ara Reaction as Diagnostic and Prognostic Aid in Cirrhosis of Liver, J. Lab. & Clin. Med. **20**:902-913 (June) 1935.

on thyroid disease in this nonendemic area,²⁷ we have observed 26 clinical cases in which death was due only to thyroid crisis; we have excluded all cases in which cardiac complications, pneumonia or any other factor played a part. We have also found 6 exactly similar cases in which autopsy revealed typical hepatic degeneration. There is every reason to believe that if the larger group of patients had also been submitted to autopsy the postmortem observations would have paralleled the clinical picture. The fact that the majority of these patients, 19 of the total group of 32, died in crisis without operation is a disturbing and impressive fact, comment on which is unnecessary.

The actual pathologic changes present in such cases at autopsy are no part of our present discussion, which concerns the fact of hepatic damage rather than the details. We may say, however, that the pathologic changes in our own cases, plus those in the cases reported in the literature, although they revealed an astonishing variety of pathologic terms apparently intended to cover the same changes, may be roughly classified as fatty infiltrative changes, degenerative changes ranging from mild changes to actual necrosis, cirrhotic changes and acute yellow atrophy. Frequently the same liver revealed various degrees of all changes in different areas, and as a rule there was a significant decrease in weight.

TESTS OF LIVER FUNCTION IN DISEASE OF THE THYROID

In view of the relation between the thyroid and the liver in the presence of toxic thyroid disease, it seems important to find some method by which the state of the patient can be estimated in terms of the hepatic factor. Clinical improvement, cardiac function, a falling basal metabolic rate—all are helpful alone or in combination, but they give no information on this point, and, as all surgeons know, they are frequently fallacious and misleading. Various attempts have been made to test hepatic function, but none with complete success. Ragins found the Takata-Ara reaction positive in 6 of 14 cases. Youmans and Warfield²⁸ found the reaction to the bilirubin test positive in 7 of 12 cases and the reaction to the dye test positive in 22 of 44 cases; in 4 of the 5 cases in which death occurred in this group hepatic damage was exhibited at postmortem examination. They noted no relation except loss of

27. Maes, U.; Boyce, F. F., and McFetridge, E. M.: Hyperthyroidism in the Negro, with Analysis of Seventy-Three Cases, *West. J. Surg.* **42**:456-463 (Aug.) 1934; Clinical Problems of Thyroid Disease in Non-Endemic Area, *Am. J. Surg.* **24**:232-253 (May) 1934; Further Observations on Thyroid Disease in a Non-Endemic Area: An Analysis of Six Hundred and Sixty-Two Surgical Cases and Sixteen Non-Surgical Deaths, *Ann. Surg.* **105**:700-716 (May) 1937.

28. Youmans, J. B., and Warfield, L. M.: Liver Injury in Thyrotoxicosis as Evidenced by Decreased Functional Efficiency, *Arch. Int. Med.* **37**:1-17 (Jan.) 1926.

weight between the functional efficiency of the liver and the clinical picture; other tests employed, including that for the basal metabolic rate, also furnished no parallels. They noted that evidence of hepatic dysfunction was most apt to be found in patients who in addition to loss of weight showed inability to maintain a satisfactory caloric intake.

Maddock, Collier and Pedersen²⁹ used the bromsulphthalein test in 13 cases of toxic goiter and found an impairment of hepatic function in 8. They noted a considerable degree of correlation between the severity of the disease, the basal metabolic rate and the degree of hepatic damage. They also found the bilirubin test satisfactory for this purpose. In their postoperative study of hepatic function they noted a gradual return to normal levels after the initial postoperative fall, but there was no correlation between the preoperative hepatic function and the postoperative course.

Hurxthal³⁰ studied 505 patients with thyroid disease by the cholesterol test. He found the values low in toxic states, elevated by the proper preoperative preparation and elevated most of all by operation. The lowest average values were for patients in or near crisis, and the next lowest, for patients with auricular fibrillation. The average values were lower with all types of exophthalmic goiter than with the nodular toxic varieties, and the values in cases of recurrent hyperthyroidism were almost as low. The average value for patients with the nontoxic condition was normal, although the scatter was wider than had been expected, which has been our experience with the Quick test. The level of the blood cholesterol and the basal metabolic rate showed an average reciprocal relationship. Adler and Lemmel (quoted by Lichtman³¹) noted abnormal cholesterol ester values in a few cases of severe exophthalmic goiter, finding the ester fraction depressed, as it tends to be with hepatic damage of other origins. Parhon and Cahane,³² studying experimental hyperthyroidism, noted a tendency toward the increase of hepatic chlorides in the experimental subjects as compared with the controls.

Althausen and Wever³³ studied 26 hyperthyroid subjects by the galactose tolerance test and found the curve much higher than for

29. Maddock, W. G.; Collier, F. A., and Pedersen, S.: Thyroid Crisis: Its Relation to Liver Function and Adrenalin, *West. J. Surg.* **44**:513-521 (Sept.) 1936.

30. Hurxthal, L. M.: Blood Cholesterol in Thyroid Disease: II. Effect of Treatment, *Arch. Int. Med.* **52**:86-95 (July) 1933.

31. Lichtman, S. S.: Liver Function in Hyperthyroidism, *Arch. Int. Med.* **50**:721-729 (Nov.) 1932.

32. Parhon, C. I., and Cahane, M.: Sur le chlore hépatique chez les animaux hyperthyroïdésés, *Compt. rend. Soc. de biol.* **120**:52-53 (May) 1935.

33. Althausen, T. L., and Wever, G. K.: Galactose Tolerance in Hyperthyroidism, *J. Clin. Investigation* **16**:257-259 (March) 1937.

normal patients; only 2 of the maximum readings were below 30 mg. The high curve, they theorized, may be due to accelerated intestinal absorption of galactose, as evidenced by the earlier appearance of galactose in the blood, but the reduced capacity to utilize carbohydrate is undoubtedly due to hepatic injury. They refused to believe that it is dependent on the low glycogen content of the liver, as most of the 14 patients with diabetes whom they studied at the same time had normal galactose curves, although such subjects usually exhibit low values for hepatic glycogen. They did not find the changes in the galactose tolerance generally proportionate to the severity of the disease. Kugelman (cited by Lichtman) found evidence of hepatic dysfunction in 10 cases studied by the levulose tolerance test.

Lichtman himself employed in 20 cases of uncomplicated hyperthyroidism the cinchophen test devised by himself and commented on in our first communication. Abnormal values were demonstrated in 16 cases, but there was no relation between the basal metabolic rate, the known duration of the disease and the loss of weight. He noted a tendency of the hepatic function to improve as the basal metabolic rate approached normal levels, but he did not find any appreciable correlation between his results with the cinchophen test, and the icteric index or the results of the galactose tolerance test, the bilirubin test or the urobilinogen test.

Schneider³⁴ has suggested that a determination of the sodium content of the blood serum will furnish an index of hepatic damage. The level is relatively constant, the norm being 281 mg. per hundred cubic centimeters. Patients with hyperthyroidism exhibit a fall in values, and operation cannot be undertaken in the presence of a level of 100 or less without grave risk. The spread seems, on the surface, rather too wide for absolute safety, and without further and stronger proof one is inclined to question his statement that the use of vitamin A will combat the fall in the glycogen content of the liver and in the sodium content of the blood serum so adequately that iodine can be dispensed with.

The tests which we have listed, most of which we described in our first communication, dealing with biliary disease, are open to precisely the same objections in thyroid disease as in biliary disease. The tests which are simple are not accurate, the tests which are accurate are usually complicated or expensive, many require repeated venipuncture, and many put an additional strain on a liver in which damage is already suspected or known to exist.

34. Schneider, E.: Concerning Broadening of Indications for Operation in Exophthalmic Goiter Through Recognition at Bedside of Secondary Thyrogenic Injury to Liver, *Internat. Clin.* 2:87-98 (June) 1934.

QUICK HIPPURIC ACID TEST OF LIVER FUNCTION IN
DISEASE OF THE THYROID

In December 1936 before the Southern Surgical Association we mentioned in a report of 321 additional cases of thyroid disease from the New Orleans Charity Hospital our preliminary studies with the Quick hippuric acid test and our conviction of its value in such cases. The paper was discussed by F. H. Lahey, who said that he also had used the test for this purpose³⁵ and had been impressed with its reliability, though he agreed with us, of course, that it could not take the place of judgment and experience in the selection of patients adequately prepared for operation.

The test has been mentioned by several writers as suitable for use in cases of thyroid disease, but we have seen only two reports in addition to our own preliminary statement. Shorr, Richardson and Wolff³⁶ used it in 6 cases of exophthalmic goiter, in all of which normal values were revealed. Without intending any implication as to its correctness in these particular cases, we might point out that many times normal values are to be expected, just as normal values are to be expected in any test for any condition. The mere fact that hepatic dysfunction sometimes occurs in association with thyroid disease does not mean that it must always occur.

The only extensive report which has appeared is by Bartels,³⁷ from the Lahey Clinic, and is an analysis of 66 cases of toxic thyroid disease studied by the Quick test. His conclusions follow: The results of the test show that liver function in the presence of hyperthyroidism undergoes a more frequent and more intense change than has previously been suspected. The changes in function correspond to the hepatic changes demonstrated pathologically and furnish an ample basis of explanation for thyroid crisis. The degree of dysfunction is related to the clinical severity of the disease and to the degree of toxicity as indicated by the basal metabolic rate and by the necessity for operation in stages. Improvement in function occurred with preoperative preparation and was more marked in diffuse toxic disease than in nodular toxic disease; the test therefore furnishes an evaluation of the success of preoperative treatment. A postoperative decrease occurred in most cases, with a later return to approximately normal. There was no correlation between

35. Lahey, F. H.: Critical Thyroid States: Their Diagnosis and Treatment, *S. Clin. North America* **16**:1521-1531 (Dec.) 1936.

36. Shorr, E.; Richardson, H. B., and Wolff, H. G.: Endogenous Glycine Formation in Myopathies and Graves' Disease, *Proc. Soc. Exper. Biol. & Med.* **31**:207-209 (Nov.) 1933.

37. Bartels, E. C., and Perkin, H. J.: Liver Function in Hyperthyroidism as Determined by the Hippuric Acid Test, *New England J. Med.* **216**:1051-1060 (June 17) 1937.

the hepatic function as demonstrated by this test and the duration of the disease or the amount of weight lost, though there was a rather close correlation between it and the increase in the cholesterol content of the blood during the preoperative preparation.

The majority of the points Bartels makes we made before the Southern Surgical Association. This test, as we pointed out at that time, is a simple method which needs no elaborate facilities or special competence. It eliminates the human equation, which invalidates determinations of the basal metabolic rate for nervous and restless subjects. It puts practically no strain on the patient and therefore can be repeated as often as necessary. On the other hand, as Bayley has pointed out in his fine study of thyroid crisis, the use of such measures as roentgen examination, venipuncture and even the basal determination of the metabolic rate may at times, however necessary they may be, precipitate a serious or a fatal crisis.

We have now used this test in a sufficiently large series of cases to make rather positive statements about it, provided, of course, it is performed with the precautions set forth in our first communication. The most important, we think, is its serial use. We believe that we can now say with a fairly high degree of accuracy that one patient is a good risk from the hepatic standpoint and another a doubtful one. By repeated tests we believe that we can safely say at the end of the planned preparation that the patient has become a good risk from the hepatic aspect, or has become a fair one, or remains a poor one and must be further prepared in anticipation of the drop in hepatic function which follows any surgical procedure. We have no doubt that in this postoperative drop lies the explanation of many deaths, particularly of improperly prepared patients, which have hitherto been attributed to other causes. We hope with further experience to be able to determine the lower limits of safety, so that we may say that some patients no matter how urgently they need surgical treatment had best be left untouched, since their lack of response to preparation presages a postoperative fall in function that is likely to be more than their badly damaged livers can endure.

We pointed out in our 1936 communication, and we would reiterate with equal emphasis here, that more should not be read into this test than it can tell. It interprets hepatic damage in terms of function; repeated tests indicate alterations in function; but a single test and repeated tests tell nothing else. This is not an index of the type of risk represented by the patient with thyrocardiac disease, for whom the cardiac damage wrought by the hyperthyroidism is the outstanding consideration. This test is no index of possible respiratory failure or of any other complication except hepatic damage. These points we shall prove later by illustrative cases.

We have to date used this test in 108 cases of surgical thyroid disease, 93 of which are shown graphically (chart 1). We also have incomplete data on 39 other cases, in many of which the patients were treated surgically. The cases shown graphically are divided as follows: diffuse goiter, 26 cases; toxic diffuse goiter, 23 cases; nodular goiter, 32 cases; nodular toxic goiter, 12 cases. The percentages of normal hepatic function are shown in the accompanying table.

The conclusions to be drawn from these figures are rather surprising. It will be noted that the response to preparation of patients with nodular toxic disease was more marked than that of patients with the toxic diffuse variety. This is the reverse of Bartels' experience and perhaps is to be explained by the difference between the varieties of thyroid

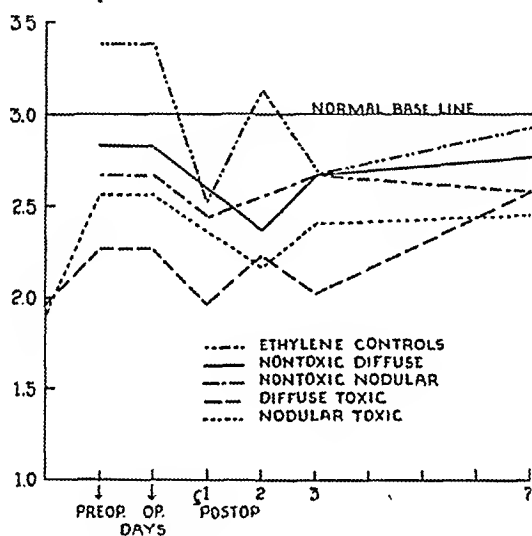


Chart 1.—Preoperative and postoperative results of the Quick hippuric acid liver function test in cases of surgical thyroid disease.

Percentages of Normal Hepatic Function

Type	Preoperative		Postoperative (by Days)			
	1	2†	1	2	3	7
Diffuse.....	83.0	52.7	70.2	79.0	81.5
Toxic diffuse.....	58.0	66.7	58.0	68.1	59.0	76.0
Nodular.....	78.8	71.8	74.0	79.0	76.0
Toxic nodular.....	57.7	76.0	69.6	64.0	71.0	72.0
Ethylene* control.....	100.0	79.0	91.0	88.5

* All thyroid operations are done under ethylene anesthesia on this service.

† After preparation.

disease in endemic and nonendemic areas. It may also be that our preparation was more intensive for the group with nodular toxic disease, which is largely composed of older Negroes, with whom we have

learned to fear trouble. The initial readings for both varieties of toxic disease are practically the same.

The marked fall immediately after operation, which parallels the fall in the control ethylene group (composed of young, normal persons submitted to elective appendectomy or hernioplasty) is as notable as the similar fall after biliary operations. The seriousness of the drop was always offset in the patients with toxic disease, and usually in those with the nodular type, who were older, by the use of infusions of dextrose. It is usually easy to determine from the figures the day on which the dextrose was withdrawn. For the simple diffuse type of goiter, dextrose was used only on special indications, and there was nothing to bolster the postoperative fall.

The relatively low values for the patients with nontoxic involvement suggests that this test may reveal a latent toxicity during which metabolism is increased and hepatic function correspondingly diminished, even though clinical manifestations are lacking. We wonder whether some such explanation does not hold for the rather marked difference in liver function between Negro and white patients (chart 2). Except in the group with toxic diffuse disease, the hepatic function at admission in terms of normal was invariably lower for the Negro than for the white patient:

Type	White	Negro
Diffuse	91.0	77.5
Toxic diffuse	55.6	59.0
Nodular	81.0	78.1
Toxic nodular	64.7	54.6

We are inclined to think that these discrepancies are something more than coincidence. In previous communications dealing with thyroid disease in this area we have commented that the Negro exhibits a rather low toxicity and is inclined to ignore his toxic symptoms, so that the duration of his disease is longer on the average than is the duration of the illness for white patients. This is not a particularly satisfactory explanation. Another curious fact is that Negro girls between 10 and 15 years of age exhibit both a relatively and an absolutely lower function, regardless of the nature of their disease, thyroid or nonthyroid, than do white girls of the same age.

In the occasional case we found a high hepatic function in the face of clinical evidence of extreme hyperthyroidism. As we have already said, our interest in dysfunction of the liver in the presence of thyroid disease does not blind us to the fact that it is not present in all cases. Again, it is possible that the anomaly may be explained by an excessive use of carbohydrates or of pure dextrose immediately before the test was performed. It may also be, as Chiray (cited by Youmans and Warfield) has suggested, that the first response of the liver to injury

may be an increase in functional efficiency. This holds true for hepatic cirrhosis and other hepatic states and may be true here also.

The practical application of the knowledge concerning the hepatic factor in thyroid disease has been demonstrated by Frazier and his associates, Brown, Frieman and North,³⁸ who have stressed the value of intravenous dextrose therapy as a prophylaxis against the violent post-operative reactions frequently seen in patients suffering from hyperthyroidism. In 70 gravely ill patients for whom they employed this therapy there were no crises and no reactions approaching crises; there

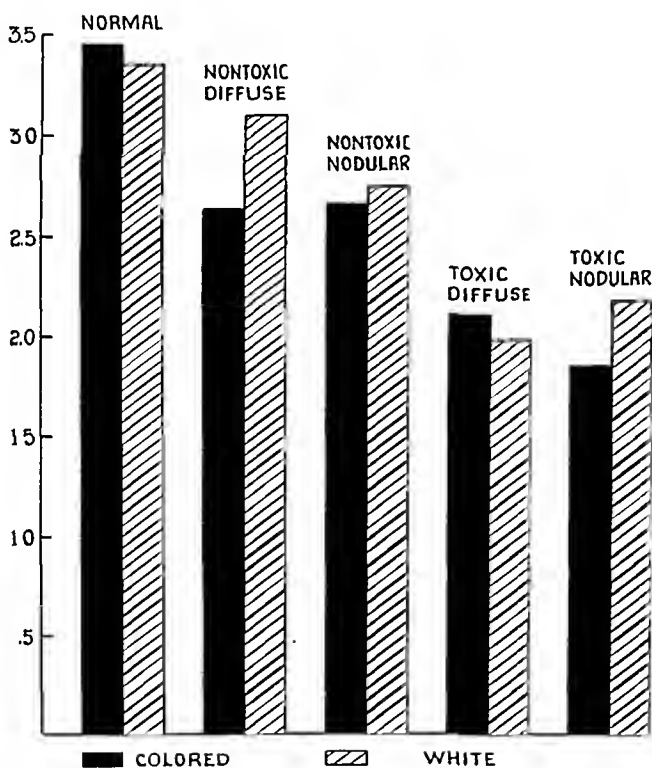


Chart 2.—Comparative study of liver function in the presence of thyroid disease, as shown by the Quick hippuric acid test performed on patients of the white and Negro races.

were also no deaths. Among a control series of 100 similar patients for whom dextrose was not used there were 2 deaths in crises, and a third patient had a similar but somewhat atypical reaction.

38. Frazier, C. H., and Brown, R. B.: *The Thyroid and the Liver*, Tr. Am. A. Study Goiter, 1935, pp. 168-178. Frazier, W. D., and Frieman, H.: *Alterations in Liver Glycogen Following Thyroid, Iodine and Glucose Feedings*, Surg., Gynec. & Obst. 60:27-29 (Jan.) 1935. Frazier, C. H., and North, J. P.: *Carbohydrate Metabolism in Hyperthyroidism*, Tr. Am. A. Study Goiter, 1933, pp. 203-209.

These same authors have stressed another important consideration, that the fatty changes frequently found in the livers of patients with hyperthyroidism are likely to be just as serious as the depletion of the hepatic glycogen, on which we have tended to focus our entire attention in the past. A high carbohydrate diet and the liberal use of dextrose will take care of the glycogen depletion, but other measures are needed to protect the organism against the equally serious fatty changes in the liver. If repeated determinations of blood sugar show that the dextrose is not being absorbed, lecithin should be added to the therapy. The persistent hypoglycemia in a case reported by Kramer and his associates and mentioned in our first communication could be explained on the basis of fatty changes in the liver, and it is possible that a similar explanation would hold in many cases of thyroid disease.

It is our own strong conviction that a large part of the decrease in the mortality from thyroid disease in Charity Hospital in 1936 as compared with the figures reported in 1933 is due to the use of dextrose in the second series. In the first 341 cases there were 26 deaths, 7.6 per cent, against 12, or 3.7 per cent, in the second 321 cases. In the first series there were 19 deaths in 177 cases of toxic disease, 10.8 per cent, against 8 deaths in the second series of 121 cases, 6.6 per cent. In the second series dextrose was used almost routinely as a postoperative measure in cases of the toxic type, as well as in many instances of nontoxic involvement. Rarely was it withheld until the need for it was demonstrated, and perhaps a still more liberal use of it would have reduced the mortality further.

The postoperative use of oxygen might also be a means of reducing the mortality caused by the hepatic factor. Judd³⁹ noted that the oxygen saturation of the blood is decreased in patients with hepatic disease and suggested inhalations of oxygen as a corrective measure. His conclusion that perhaps one result of transfusion is to improve the oxygen saturation curve seems entirely rational, and both oxygen therapy and transfusion would seem indicated for toxic thyroid disease in which the hepatic factor is apparent.

The following cases present several points of interest.

CASE 1.—An exceedingly toxic Negro aged 37 entered the hospital with congestive heart failure and a two year history of toxic (diffuse) thyroid disease. Preparation for surgical treatment was complicated by the necessity for thoracentesis and the extreme difficulty of keeping him in bed and submissive to the regimen ordered for him. At the time of his admission the Quick test reading was 1.221, approximately 35 per cent of normal. Before the first lobectomy, for which he was prepared by standard treatment (including dextrose therapy) the value had risen to 2.523. He stood the operation well; he was given dextrose

39. Judd, E. S.; Snell, A. M., and Hoerner, M. T.: Transfusion for Jaundiced Patients, *J. A. M. A.* 105:1653-1658 (Nov. 23) 1935.

liberally for several days afterward, and after the expected postoperative drop the test of hepatic function showed almost the same reading as before. Because his cardiac condition made him a very poor risk, the second operation was delayed as long as possible, but the recurrence of the toxic symptoms, together with evidence of failing hepatic function by serial Quick tests, clearly indicated the necessity for the second lobectomy.

He was prepared for it with even more difficulty than for the first, partly because of the confusion incident to the demolition of the old Charity Hospital and the removal of the patients to other quarters. Then, two days before operation was to be done, through a most unfortunate error he was dismissed from the ward by a house officer charged with the task of clearing the hospital of all patients except those in urgent need of treatment, during the actual days of moving. The error was promptly discovered, and the patient was brought back to the hospital from the country four days later. He was in very poor condition, however, especially from the cardiac aspect. Again he was prepared for operation, and when this was undertaken ten days after his return, his hepatic function, which had fallen to 1.461 during his absence from the hospital, had risen to 2.974, though the cardiac state was extremely unsatisfactory. His immediate reaction from the second lobectomy was not alarming, but congestive cardiac failure developed on the second day, and he died within forty-eight hours. Permission for autopsy could not be secured. We have quoted this case at length because it illustrates two points. The first is the correlation between clinical improvement and regression and the elevation and fall in the Quick test readings. The second is the uselessness of the test as an indication of cardiac risk.

CASE 2.—A Negress aged 36 was admitted to the hospital with typical symptoms of nodular toxic goiter. She had been treated with iodine for an undetermined period before admission. In her first test of hepatic function the reading was 1.950, and in the second, five days later, 1.114, the decrease corresponding to the extremely nervous state to which she had been reduced by the noise and confusion incident to the demolition of the hospital. During intensive preparation of the patient for the operation the function rose to 2.789, and she seemed so good a risk that subtotal thyroidectomy was done instead of the lobectomy which had been originally planned. She reacted well. Three hours later, just as an intravenous infusion of dextrose was about to be given, with a normal blood pressure, a pulse rate of 90, a temperature of 99 F. and a respiratory rate of 22, she suddenly stopped breathing and could not be revived. The patient was under observation when the catastrophe occurred. There was no evidence of hemorrhage, nor could any other accident be demonstrated as a possible cause of death. Autopsy was not permitted. The hepatic factor clearly played no part in this death, and, again, such a fatality cannot be predicted by the Quick or by any other test for hepatic function.

CASE 3.—A white woman aged 43 was admitted to the hospital with a toxic nodular goiter and signs of extreme toxicity. The initial hepatic function of 1.859 rose to 3.425 after intensive preparation, including dextrose therapy. Operation was done in stages, in spite of the improvement. The hepatic function after operation was well maintained until the fourth day, when dextrose was withdrawn. Then it fell to 1.796, although it rose gradually thereafter, and convalescence was without incident. She returned for the second operation two months later, at which time the initial hepatic function was 3.012 and her clinical condition was greatly improved. After proper preparation the second lobectomy

was done, without complications. Again the tests of hepatic function, after the initial postoperative drop and the further drop when dextrose was withdrawn, kept pace with the clinical improvement.

This case furnishes an excellent illustration of the value of the test as an index of the efficacy of preoperative preparation, as well as of the improvement in function which follows properly performed operations. Clinically the patient on admission was a very poor risk.

SUMMARY

Clinical and experimental proof of the relation between the liver and the thyroid is presented.

The tests of hepatic function previously used in thyroid disease are discussed.

Our own experience with the Quick hippuric acid test of hepatic function as applied to thyroid disease is outlined.

The conclusions possible from our results are discussed.

Illustrative cases are cited.

STUDIES OF HEPATIC FUNCTION BY THE QUICK HIPPURIC ACID TEST

III. VARIOUS SURGICAL STATES

FREDERICK FITZHERBERT BOYCE, M.D.

AND

ELIZABETH M. McFETRIDGE, M.A.

NEW ORLEANS

In two previous communications¹ we have discussed the value of the Quick hippuric acid test of hepatic function in the treatment of hepatic and biliary disease and of thyroid disease. In this communication we shall consider it in connection with the general problems of surgery. We are increasingly of the opinion that the role of the liver in all types of surgical disease is more important than is generally suspected, and we are in hearty accord with the writers—they are relatively few—who make the point that it is quite as important to consider the liver in evaluating the surgical risk as it is to consider the heart, the kidneys and the lungs.

In our first paper on the subject of "liver death," which was written in 1934, we said:

Our experimental study has not yet progressed to the point at which we feel that we can make suggestions of any value to prevent the distressing catastrophe of "liver death." The most important consideration, it seems to us, lies in Graham's rather casually uttered statement that . . . the patient with a damaged liver presents a questionable risk not only for operation on the biliary tract, but for any operation, no matter how trivial it may be . . . that warning, taken at its face value, will mean for all practical purposes a surgical revolution. It will mean that there will be no more "simple surgery." It will mean, particularly, that the surgeon who proposes to perform operations on the biliary tract . . . must regard all such patients as presenting potentially poor risks, regardless of how incongruous their inclusion in such a category may seem. It means, to go further, that all candidates for any operation must be studied from the standpoint of hepatic function, and that the ninety and nine must be discommoded and inconvenienced to rescue the one who may otherwise be lost.

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1. Boyce, F. F., and McFetridge, E. M.: Studies in Liver Function by the Quick Hippuric Acid Test: I. Biliary and Hepatic Disease, *Arch. Surg.*, this issue, p. 401; Studies in Liver Function by the Quick Hippuric Acid Test: II. Thyroid Disease, *ibid.*, this issue, p. 427. These papers contain extensive lists of references, which are not repeated here.

When those words were written we were unaware of Shallow's statement to the same effect, though actually, as Robertson pointed out, he seems to have been one of the very first to be emphatic about the matter. In the course of a staff meeting he mentioned a certain unexpected mortality in his surgical practice, the reason for which became clear when dye retention tests for hepatic function revealed in many cases damage of which there had been no clinical evidence. In the light of those findings he adopted the principle that patients who reveal such damage and who do not respond to standard measures to correct it had best be refused all but emergency operations.

The data on patients whom we have studied as controls in our work with the Quick hippuric acid test bear out Shallow's contention. For most of the 28 presumably normal patients whom we studied the test readings were normal, as were those for the normal subjects studied by Vaccaro, Quick, Kohlstaedt and Helmer, and Yardumian and Rosenthal. Yet at intervals we found patients normal by every clinical standard who revealed unexpectedly low values in this test. Such patients we are inclined to look on with dubious eyes unless they are definitely prepared for their surgical ordeal, for our controls show that even entirely normal persons undergo a more or less marked drop under all types of anesthesia.

Knowledge of the effect of anesthesia on the liver is, of course, not new. The work of Rosenthal² and of Bourne,³ to mention only one group of workers in this field, has made it clear that ether as well as chloroform causes an impairment of hepatic function as measured by the dye test. Bourne wrote:

The striking difference between the ether and chloroform results is that with the former the animal has returned to normal the next day, while with chloroform the harm continues to progress, and does not reach a maximum until the day after the anesthesia.

Our findings are also more striking than those of Cantarow, Gartman and Ricchiuti.⁴ Studying 60 patients on whom cholecystectomy was performed for biliary disease without jaundice, they found by the bilirubin and the dye retention test evidence of postoperative impairment of hepatic function, which sometimes lasted four days.

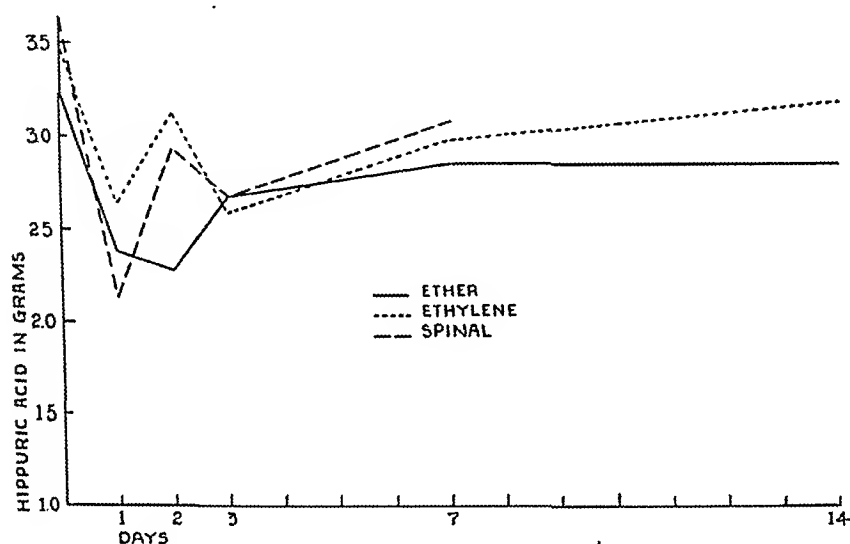
Our findings with the Quick test, as we have said, are rather more striking. For purposes of comparison with our groups of patients operated on for disease of the thyroid gland or of the biliary tract, we

2. Rosenthal, S. M., and Bourne, W.: The Effect of Anesthetics on Hepatic Function, *J. A. M. A.* **90**:377-379 (Feb. 4) 1928.

3. Bourne, W.: Anesthetics and Liver Function, *Am. J. Surg.* **34**:486-495 (Dec.) 1936.

4. Cantarow, A.; Gartman, E., and Ricchiuti, G.: Hepatic Function, *Arch. Surg.* **30**:865-874 (May) 1935.

elected to study as controls (see chart) groups of presumably normal persons who were to undergo elective operations (appendectomy and hernioplasty) for conditions not connected with the biliary tract or the thyroid gland, in order to note the effect on hepatic function of supposedly simple operations. These patients were not specially prepared for operation, nor were they given special postoperative treatment; only patients who made an uneventful convalescence were included. It is interesting and surprising, as we have implied in previous communications, to note what anesthesia and simple operations do to the liver, as expressed in percentages of normal function (table 1).



Preoperative and postoperative results of the Quick hippuric acid test for liver function in uncomplicated appendectomies and hernioplasties performed with various types of anesthesia.

TABLE 1.—Percentage of Normal Function

Anesthetic	Admission	Postoperative (by Days)				
		1	2	3	7	14
Ethylene.....	100	79	91.0	88.5
Ether.....	95	70	67.4	79.3	83.4	83.4
Spinal.....	111	62	87.0	79.0	90.1	92.0

On the basis of these figures, the Quick test would seem to be a more delicate index of hepatic function than either the bilirubin test or the dye test, which were used in the studies just referred to.

There are many possible explanations for the 25 per cent drop in hepatic function with ether anesthesia. Crile, for instance, showed the serious consequences of exposure of the liver during abdominal

operations and said that the deleterious effects are enhanced when ether anesthesia is used. With each degree of falling temperature, he stated, there is a loss of 10 per cent in hepatic efficiency. He suggested the use of diathermy during operation as well as during the critical days after the operation, to take care of the thermal factor. He also suggested that a less dangerous anesthetic than ether be used.

Mann and his associates have shown that the hyperglycemia which occurs after ether anesthesia is the result of a loss of glycogen from the liver. Mann has also shown that ether decreases secretion of bile and depresses other hepatic functions, notably the formation of urea.

From another standpoint, Bourne's experiments have shown that when inhalation anesthetics, even such safe ones as nitrous oxide and ethylene, are administered without adequate oxygenation the experimental animals suffer an impairment of hepatic function which requires several days to overcome. Shaw, Steele and Lamb⁵ have shown in recent elaborate studies on ether anesthesia the existence of anoxic anemia and have suggested that oxygen be administered coincidentally with the anesthetic to secure a normal oxygen saturation of the arterial blood. The work of Goldschmidt, Ravdin and Lucke⁶ is to the same purpose. By volatilizing the anesthetic with oxygen they were able largely to prevent the necrotizing effect on the hepatic cells usually produced by such an agent as chloroform or divinyl ether. They also found that a high carbohydrate diet before operation had much the same effect. Their theory, based on experimental evidence, is that the improvement which occurs in the portal circulation as the result of inadequate oxygenation may play an important part in the result. This would be in line with Judd's idea, which we have mentioned in our earlier communications, that hepatic dysfunction is associated with defective oxygenation of the blood.

It must be remembered that these normal patients, even though they are not formally prepared for operation, do undergo a period of starvation or semistarvation, sometimes for as long as twelve or fourteen hours. The work of C. S. Stone, which we mentioned in our first paper on the Quick test, is applicable here. Working with partially hepatectomized rats which had been fed a high carbohydrate diet, he found that if the animals were killed when the stomach was full the glycogen level was high, whereas if they were killed when the stomach

5. Shaw, J. L.; Steele, B. F., and Lamb, C. A.: Effect of Anesthesia on the Blood Oxygen, *Arch. Surg.* **35**:1-10 (July) 1937.

6. Goldschmidt, S.; Ravdin, I. S., and Lucke, B.: Anesthesia and Liver Damage: I. The Protective Action of Oxygen Against the Necrotizing Effect of Certain Anesthetics on the Liver, *J. Pharmacol. & Exper. Therap.* **59**:1-14 (Jan.) 1936.

was empty the hepatic glycogen values were low. The early experiments of Whipple and his associates on hepatic damage produced by chloroform showed that the full effect of the anesthetic on the liver could not be felt unless the animals were starved before its administration. In recent (unpublished) experiments of our own we have duplicated these findings and have been impressed with the prompter and more extensive damage produced in the liver when the chloroform was given to starved animals. Unquestionably the administration of the anesthetic after the period of starvation plays some part in the drop in hepatic function after operation.

It is a striking fact that although the patients operated on under spinal analgesia showed the highest initial values—all of them were young, vigorous men—they also showed the greatest postoperative fall, 49 per cent. For most of them the operation performed was hernioplasty, which does not involve extensive exposure of the abdominal contents, or appendectomy through a McBurney incision, of which the same may be said.

There are many explanations for this drop, some of them probable, some of them purely speculative. It is reasonable to assume that the fall in blood pressure which is known to occur with spinal analgesia may result in a decreased oxygen supply to the liver. If this is so, it is entirely possible that the postoperative decrease in hepatic function is at least partly due to an anoxemia, exactly as with inhalation anesthesia, in connection with which we have already pointed out the results of inadequate oxygenation.

Another explanation of the postoperative drop after spinal analgesia is perhaps found in the fact that the drugs used to secure it, like the drugs used to secure local analgesia, are largely eliminated in the liver. Heyd noted that anesthetics given by rectum or by colon are eliminated in the same way; he warned against using them and adding further insults to the liver when hepatic damage is known or suspected to exist. He too stated that nitrous oxide or ethylene with the addition of very small amounts of ether is the safest of all anesthetics.

The dangerous possibilities inherent in spinal analgesia have long been realized, and our findings in this test make those risks doubly impressive. A recent study by Veal and Van Werden⁷ from Charity Hospital may be quoted in this connection. In a study of 30 fatalities directly attributable to spinal analgesia they found that 19 of the deaths occurred in the presence of such abdominal conditions as intestinal obstruction, peritonitis, gunshot wounds, hepatic abscess and cholecystitis.

7. Veal, J. R., and Van Werden, B. deK.: Mortality of Spinal Analgesia Based on an Analysis of Thirty Immediate Fatalities in a Series of 33,811 Cases. *Am. J. Surg.* 34:606-610 (Dec.) 1936.

These are all conditions in the presence of which it is not unreasonable to postulate some degree of hepatic damage, particularly when one recalls the advanced stage of illness at which many patients are seen. We have no tests on these patients to prove our point, but it is not unreasonable to assume that the fall in hepatic function after the administration of the spinal analgesia may have had something to do with the fatal outcome.

In a recent study of 715 cases of acute intestinal obstruction from Charity Hospital⁸ we found further indirect proof of the possible effect of spinal analgesia on the liver. In 9 of these cases hepatic damage was apparent as the only cause of death, and 6 of the 9 patients had had spinal analgesia. We have no tests to prove the point, but it is permissible to draw attention to what may be a coincidence but may also be a cause and effect relation. We suggest that the same fall in hepatic function noted in healthy subjects after operation and withstood by them might have occurred with disastrous results in patients with intestinal obstruction whose livers were already damaged—there is no doubt of that damage in certain cases of obstruction. All these patients died promptly, with hyperpyrexia or with uremic symptoms typical of “liver death” or the “liver-kidney syndrome.” Whether or not our presumptions are sound, we are certainly justified in saying that spinal analgesia is not the safe anesthetic it is usually supposed to be. If ethylene could give the proper relaxation it would seem to be the safest anesthetic of all. We have had no experience with cyclopropane, but in view of the high admixture of oxygen which it permits, it would also seem a very safe agent.

It is regrettable that the Quick test is not applicable to patients with intestinal obstruction, for it should furnish some interesting results. Such patients, of course, cannot safely be given fluids by mouth, nor can they be deprived of fluids by other routes for the period necessary to the test. Del Rosso⁹ reported 7 cases of intestinal obstruction studied by the rose bengal test, in all of which there was a high retention of the dye, and we regret that we cannot duplicate his studies with the Quick test.

In connection with our studies in anesthesia we report an interesting case:

A young and vigorous man, 18 years old, was operated on in July 1937 for an indirect inguinal hernia on the left side. It was causing no symptoms, but

8. Boyce, F. F., and McFetridge, E. M.: *Acute Intestinal Obstruction*, *South. Surgeon* 6:109-125 (April) 1937.

9. del Rosso, L. M.: *La funzionalità epatica, nell'occlusione intestinale acuta, studiata con il rosa bengala (Contributo clinico e sperimentale)*, *Policlinico (sez. chir.)* 40:224-236 (April) 1933.

he had been refused admission to a CCC camp until it was corrected. The routine tests and the urea clearance test gave normal values. Operation was done under ethylene anesthesia and took forty minutes. The preoperative hepatic function was 3.726; on the first day after the operation it was 2.801 and on the fourteenth 3.222.

The patient was readmitted to the hospital at the end of September with a story of several recurrent attacks of appendicitis during the interval. We were not aware of the readmission, and the Quick test was ordered by the intern without our knowledge, because, as he told us, the man had so many complaints he thought he would furnish him with something to complain about. It was well that he had this inspiration, for the studies on this patient were most interesting. The value on admission was practically what it had been on his discharge ten weeks before, 3.205. Appendectomy was done with the patient under ether anesthesia, through a right rectus incision, and took forty-five minutes; the appendix was retrocecal and contained one fecolith. On the first day after the operation the patient was perfectly well; he had not vomited; there was no distention; the temperature, the pulse rate and the respiratory rate were within normal limits, but the hepatic function value had fallen to 1.891. On the fifth day it had risen to 2.449 and on the seventh to 3.022. The marked difference between the values revealed by the Quick test after the use of different anesthetics and after different procedures is so obvious as to need no comment.

Another interesting problem is furnished by an 80 year old patient who was submitted to hernioplasty and orchidectomy. Routine laboratory tests showed normal values, as did the urea clearance test, and the Quick test showed a reading of 2.9. In spite of the excellent hepatic function, we suggested that because of the patient's age ethylene be used for the operation. On the first day after the operation the Quick test was 2.035, and it had reached only 2.434 on the seventh. It is interesting to speculate what the postoperative drop might have been for this aged subject had ether or spinal anesthesia been used.

The lesson to be derived from these observations is clear. Even elective operations on sound subjects result in an impairment of hepatic function, against which it might be well to guard by such simple measures as the oral administration of carbohydrates, particularly dextrose, before and immediately after operation. We have previously quoted the work of Althausen to show the efficacy of dextrose administered by this route. It seems particularly wise to do this as a matter of routine because of the occasional unexpected death which follows even elective operations on supposedly sound persons. A recent death in our own service illustrates this point:

A Negroess aged 19 was operated on under ether anesthesia for recurrent appendicitis. The appendix was retrocecal and rather difficult to remove. It was noted that the patient did not recover well from the anesthetic, remaining drowsy and listless most of the day. The following morning she seemed better, but thirty-one hours after operation the temperature began to rise, and she died six hours later, with an axillary temperature of 105.6 F. She did not respond

to infusions of dextrose. Permission for autopsy was refused, but there was no clinical evidence of shock, hemorrhage or anything else to explain why she died. Perhaps a preoperative study of the hepatic function might have revealed an unexpected deficiency, and steps could have been taken to guard against the catastrophe.

Some of the other cases (some 40 in all) which we have studied by this test are set forth in table 2 and need only casual comment. Not much work, so far as we can determine, has been done with hepatic function tests in cases of splenic disease. Greene and his associates, who used the dye test, considered it of value in relation to the severity of cirrhotic changes in the liver and therefore of some value prognostically and diagnostically. Most of the other tests they employed gave negative results, and they considered the bilirubin test of value as an index rather of the severity of the hemolytic process than of hepatic impairment.

In both cases of carcinoma of the pancreas reported by Quick, the hepatic function was less than 50 per cent of normal. In all our 6 cases the function was reduced, in some instances to 20 per cent or less of normal values. One case (case 6) bears out our repeated contention of the value of dextrose. We reported the patient safe for operation, and after intensive preoperative preparation with both oral and intravenous use of dextrose, cholecystenterostomy was performed, from which, in spite of his age (70 years), he made an excellent recovery. Dextrose therapy was continued intensively for eight days after operation, and the hepatic function was actually higher on the seventh day after the operation than it had been before operation. Both subsequent tests showed a considerable drop, unquestionably, we believe, because the intensive dextrose therapy was withdrawn and the full effect of the operation was felt.

The single case of benign pancreatic disease (case 11) is also interesting, but unfortunately operation was done before we began to use the test serially, and our studies are therefore inadequate. The patient, a Negro aged 51, was a poor surgical risk. The preoperative value for hepatic function was 1.437. Intensive dextrose therapy was given in preparation, and cholecystgastrostomy was done with the patient under ethylene anesthesia, for what was considered to be carcinoma of the head of the pancreas. The diagnosis was made chiefly on the basis of the stony hardness of the growth, although the absence of gross metastasis was commented on and was explained by the character of the disease observed at autopsy.

The patient's postoperative condition was never anything but hopeless, but it was a matter of extreme interest to us to study his urinary function in connection with the influence of decholin sodium (sodium

TABLE 2.—*Various Diseases*

No.	Race	Sex	Age	Diagnosis	Quick Test	Comment
1	White	Female	31	Banti's disease	3.025 3.748 2.443	Preoperative After splenectomy, 4th and 6th days Intensive dextrose therapy
2	White	Male	22	Banti's disease	1.168 2.424 3.150 2.4	Preoperative After splenectomy, 1st, 2d, 3d and 8th days; intensive dextrose therapy, withdrawn 5th day
3	White	Male	49	Banti's disease	2.129 1.325 2.088	Preoperative After splenectomy, 7th and 14th days, after dextrose had been discontinued
4	White	Male	61	Tuberculosis of spleen	2.474 0.778 0.535 1.462 1.752 1.837	Preoperative After exploration, 1st, 2d, 3d, 7th and 14th days
5	White	Male	71	Carcinoma of head of pancreas	1.708 1.94	Preoperative; icteric index 66.6; transfusion Fourteen days after cholecyst-gastrostomy
6	Negro	Male	70	Carcinoma of head of pancreas	2.469 2.72 2.017 1.491	Preoperative; icteric index 100; dextrose preparation After cholecystgastrostomy, 7th 10th and 14th days; dextrose withdrawn 9th day
7	White	Male	64	Carcinoma of head of pancreas	1.174 0.429 1.222	Operation refused; patient left hospital; icterus index 166 Return 6 weeks later Fourteen days later; daily dextrose infusions; autopsy confirmed diagnosis
8	White	Female	45	Carcinoma of head of pancreas	0.490	Inoperable; icterus index 111
9	Negro	Male	73	Carcinoma of head of pancreas	0.716	Operation refused; icterus index 160
10	White	Male	54	Carcinoma of head of pancreas	2.413	Clinical diagnosis; operation refused
11	White	Female	69	Carcinoma of head of pancreas	0.636	Refused operation; icterus index 125
12	Negro	Male	51	Cystic disease of pancreas	1.457 0.512	Preoperative; icterus index 160 Nineteen days after cholecyst-gastrostomy; liver-kidney death 10 days later; repeated improvement in uremic symptoms after decholin therapy
13	White	Male	60	Gastric carcinoma	2.256	Hepatic metastasis; exploration
14	White	Male	61	Gastric carcinoma	2.501	Hepatic metastasis; exploration; sudden death (embolism) 23 days after operation
15	White	Male	49	Carcinoma of rectum	0.615 1.407 0.614 1.057 0.699 0.522	Preoperative After preparation 1st day after colostomy 3d day after colostomy Jaundice; icterus index 160 Three weeks ante mortem; autopsy refused
16	White	Female	63	Diabetes	2.642	After stabilization
17	White	Female	63	Diabetes	1.409 2.172	Blood sugar 265 Stabilization begun
18	White	Male	51	2d degree burns, small area	2.601 3.558	Three days after admission Twenty-eight days later

TABLE 2.—*Various Diseases—Continued*

No.	Race	Sex	Age	Diagnosis	Quick Test	Comment
19	White	Female	47	2d degree burns, one fourth body area	1.903	Three days after admission
					2.192	Four days later
					2.791	Three months later
20	Negro	Male	48	Multiple myeloma	1.817	
					1.430	
21	White	Female	44	Cardiac disease	2.835	Compensated
22	White	Male	28	Malaria	3.368	After treatment
23	White	Male	26	Urethritis	3.754	
24	Negro	Female	19	Sickle cell anemia	2.011	
					1.889	Two weeks later
25	White	Female	46	Dyspepsia of unde- termined origin	2.540	
					1.980	Fourteen days after explora- tion under ether; negative findings
26	White	Female	69	Dermoid cyst of neck	2.193	
					1.990	Fourteen days after removal under ethylene, operation lasted 2 hours
27	White	Female	28	Salpingitis	3.615	

dehydrocholate) on his hepatic function. The urea content of the blood rose steadily, reaching 88 mg. per hundred cubic centimeters just before his death, but again and again when it rose to abnormally high levels and uremic symptoms appeared, injections of decholin reduced it and eliminated the symptoms temporarily. He finally died on the twenty-fifth day after operation with progressive anuria. Autopsy showed cystic disease of the pancreas, associated with a marked degeneration of the liver. In our study of the Quick test for patients with biliary disease we have discussed at length the relation between urinary output and hepatic dysfunction, and it is unfortunate that we did not make repeated tests in this case. On the other hand, the second test, performed fourteen days after operation and eleven days before death, showed much impaired hepatic function (0.812).

One of the 2 cases of carcinoma of the rectum (not listed) deserves special comment. The patient was studied at intervals for two months, during which time biopsy of material taken from the rectum was done, colostomy was performed and exploration was made in the hope that resection of the growth might be possible. All the operations were done with the patient under ether anesthesia. The initial hepatic function value was 3.140, and it was interesting to observe the fall and rise after each operation. Particularly notable was the fall of 50 per cent after the first operation, in which biopsy of material from the rectum was done but postoperative dextrose therapy was not given, as compared with the fall of only 28 per cent after the second, in which colostomy was

done and intensive postoperative dextrose therapy was instituted. The patient died three months after the third operation, and autopsy, which revealed the liver entirely free from metastasis, explained why the hepatic function had remained unimpaired.

Bargen and his associates studied by the dye test 116 cases of carcinoma of the colon and rectum, in which ascites was not present. In half the cases the presence of hepatic metastases, which they had suspected clinically, was confirmed by the evidence of hepatic impairment furnished by this test. In the other cases, although the liver was not palpable, the impaired hepatic function revealed by the test was confirmed at operation when the surgeon found the liver riddled with metastases. The direct van den Bergh reaction did not occur constantly enough in this series to be of diagnostic value. Bargen suggested that in the occasional case a test of hepatic function may reveal unsuspected metastasis and spare the patient a useless and perhaps lethal exploration. We are not yet sufficiently convinced of the accuracy of the Quick test, or of any other, to direct our therapy by its results.

We have studied hepatic function by the Quick method in 4 cases of burns. In this type of case one is handicapped by the fact that the most seriously injured persons, in whom most extensive hepatic damage would be likely to occur, cannot safely be deprived of fluids for the period necessary for the test. All of these burns were of moderate degree, but for all patients the initial test showed lowered values, the readings ranging from 2.601 for the least extensive to 0.890 for the most extensive injury. The last mentioned case (not listed) is worth reporting. The test was repeated at intervals over a period of twenty-eight days while the patient was recuperating from the burn. Convalescence was satisfactory, but on only one occasion did the value rise to 2.663; the rest of the time it did not rise above 1.8. On the twenty-eighth day she suddenly showed acute abdominal symptoms, for which operation was done ten hours later, after a diagnosis of mesenteric thrombosis had been made. Extensive resection of the small bowel was necessary. After a brief period of remarkable improvement she grew rapidly worse. She died on the tenth day after the operation. Autopsy showed localized peritonitis, which perhaps was sufficient to explain her death. On the other hand, degenerative changes were present in the liver, and the markedly impaired hepatic function may have played some part in the fatal result.

We have used the test in so few cases of pregnancy that we are unprepared to comment on it personally except to say that if the nitrogen retention in the blood is high, as it was in 2 of our cases, the Quick test must be interpreted with this fact in mind. Kohlstaedt and Helmer used the test in 5 cases of toxemia of pregnancy and found the values

generally low. Hirscheimer used it for 25 patients and found that even normal pregnant women showed an impairment of function near term. Toxic patients showed a more marked drop. In most cases normal values were reached during the puerperium. His findings corroborated the studies of Sullivan, Tew and Watson, he noted, with the bilirubin and dye tests. He pointed out also that the dietary treatment usually given for the toxemias of pregnancy may increase instead of improve the hepatic impairment and suggested as a substitute the intensive use of aminoacetic acid.

Of the miscellaneous cases we have studied, only 1 (not listed) is worth special comment. A Negress aged 45 was sent to us from the gynecologic service for the investigation of a mammary tumor following hysterectomy, convalescence from which had included a rupture of the wound, with resuture. The initial reading was 0.698, and as she refused further surgical treatment we have no other report on her. This case is to be compared with one reported in our first paper, on the group of patients submitted to operations on the biliary tract. This patient, a man aged 36, made an excellent recovery from cholecystectomy for chronic cholecystitis, except that he had a persistent cough. His hepatic function was 3.205 before operation and 2.400 on the seventh day after the operation. On the tenth day he suffered a rupture of the wound with extensive evisceration; resuture under local analgesia was done fourteen hours later. The hepatic function three days after the second operation had fallen to 1.726, though it was practically normal again when he was discharged. It will be interesting to study other cases of evisceration, to determine whether such lowered readings are accidental or are constantly associated with this complication. If they are, they may explain some of the deaths which follow it.

Kohlstaedt and Helmer suggested the Quick test as a method of evaluating the possible risk of the therapeutic use of such hepatotoxic drugs as arsphenamine. The incidence of jaundice in patients treated by this method, they pointed out, has been shown by Wile and Sams to be 1.3 per cent, against an incidence of 0.18 per cent in untreated patients. We have no complete studies on patients with this sort of condition, nor have we any on patients with arsenic poisoning, such as Heyd described. In support of his idea that retained arsenic may be a factor in hepatic degeneration he mentioned 3 patients in whom the condition was identified within a relatively brief period at the Postgraduate Hospital, all admitted for nonbiliary disease. The figures of Vogel, which he cited, showed an excess of arsenic in the secretions of 34 of 40 jaundiced patients; 9 of the 34 patients died. Heyd's theory is that the wide use of arsenic as an insecticide and in the dyeing and textile trades, as well as the presence of minute quantities

in cooking utensils and city dust, makes this possibility not as fantastic as it sounds. The Quick test might be of value in suspected cases of this sort.

SUMMARY

The results of the Quick hippuric acid test for hepatic function have been analyzed in a series of presumably normal subjects on whom simple elective operations were done, various types of anesthesia being used.

In all cases there was a marked drop in hepatic function after operation, the impairment being most marked with spinal analgesia and least marked with ethylene anesthesia.

The possible causes of this postoperative drop are discussed, and the wisdom of preparing all patients for operation, regardless of how normal they may seem and how simple the procedure may be, is pointed out.

The results of the test in a miscellaneous group of cases, including cases of intestinal obstruction, of splenic disease, of malignant tumor of the rectum, of pancreatic disease and of burns, are discussed.

Other possible uses of the Quick test are suggested.

TREATMENT OF INTRACTABLE BRONCHIAL ASTHMA BY BILATERAL RESECTION OF THE POS- TERIOR PULMONARY PLEXUS

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AND

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Although it is relatively small, there exists a group of patients afflicted with typical bronchial seizures which are unamenable to medicinal therapy. It is to the amelioration of these attacks in such patients that our attention has been drawn. Only cases of unquestionable bronchial asthma have been selected, and only patients totally incapacitated physically have been subjected to operation. The rationale of the procedure of bilateral resection of the posterior pulmonary plexus is based on the anatomic fact that only at this point can the extrinsic nerve supply of the lung be completely interrupted. The preganglionic efferent fibers of both the vagus and the sympathetic bronchomotor tracts from the same and contralateral sides, together with the sensory or afferent fibers emerging from the lung, form a rather limited anastomosing plexus on the posterior surface of the hilus of the lung. By resection of this plexus it is therefore possible to isolate the entire organ from any influence brought to bear on the lung through its extrinsic nerve supply. Physiologic observations made both in the past and recently have shown beyond question that bronchoconstrictor fibers are distributed mainly in the branches of the vagus nerve to the lung of the same side and that of the opposite side and to some extent accompany the sympathetic fibers. Sensory fibers from the lung, whose ganglions are to be found mainly in the ganglion nodosum, run principally in the vagi but also to some extent in the sympathetic trunks. By various experimental methods of stimulation of the proximal and distal ends of the divided vagi and sympathetic trunks as well as of the intact nerves, pronounced narrowing of the air passages of the lungs has been produced. Further reference to this will be made.¹

From the Surgical and Medical Clinics of the Johns Hopkins University.

1. Longuet, F. A.: *Anatomie und Physiologie des Nervensystems des Menschen und der Wirbeltiere*, translated by J. A. Hein, Leipzig, Brockhaus & Avenarius, 1849, p. 247. Volkmann: *Nervenphysiologie, Handwörterb. d. Physiol.* 2:586, 1844. Riegel, F., and Edinger, L.: *Experimentelle Untersuchungen zur*

(Footnote continued on next page)

The selection of patients for this method of treatment depends on the severity and frequency of the asthmatic seizures. Therefore, a most careful diagnostic survey is essential, and less radical measures should first be carried out in an attempt to relieve the patient.

Those of our patients for whom this method of treatment was used had been under observation in the asthma clinic of the Johns Hopkins Hospital for many months. They were thoroughly examined for causes of asthma, and when a suspected cause was discovered effort to relieve the patient was made by administration of the appropriate treatment. All foci of infection were removed; the patient was frequently hospitalized to tide him over a period of violent asthmatic paroxysms, and when such treatment was indicated specific antigens were given subcutaneously in an attempt to desensitize the patient to the offending agent. Only in cases in which it was felt that the recurring severe and prolonged asthmatic attacks might cause the death of the patient did we recommend operative intervention.

This report covers the treatment of 11 patients who were repeatedly in a condition of status asthmaticus before operation and who were consequently economically and socially completely incapacitated. The first patient was operated on in March 1934 and the last in March 1936. Our observations cover a maximum period of three years and nine months and a minimum period of one year and nine months. Five additional patients have been operated on since March 1936, 3 of whom at the time of writing have remained completely well for one year and 2 of whom remain improved after a shorter period. However, it is felt that the period of observation in their cases is not long enough to permit the drawing of definite conclusions. No deaths which could be attributed to the operative procedure have occurred.

OPERATIVE TECHNIC

The patient is placed on the operating table in the semiprone position, and the side to be operated on is elevated by means of a sand bag placed beneath the anterior thoracic region. The arm is allowed to fall to the side and is loosely fixed at the table edge. After the skin has been prepared by careful cleansing with ether, a 3.5 per cent solution of iodine

Lehre vom Asthma, *Ztschr. f. klin. Med.* 5:413, 1882. Einthoven, W.: Ueber die Wirkung der Bronchialmuskeln, nach einer neuen Methode untersucht, und über Asthma nervosum, *Arch. f. d. ges. Physiol.* 51:367, 1891. Beer, T.: Ueber den Einfluss der peripherem Vagusreizung auf die Lunge, *Arch. f. Physiol.*, 1892, supp., p. 101. Dixon, W. E., and Brodie, T. G.: Contributions to the Physiology of the Lungs: I. The Bronchial Muscles, *J. Physiol.* 29:97, 1903. Weber, E.: Neue Untersuchungen über experimentelle Asthma und über die Innervation der Bronchialmuskeln, *Arch. f. Physiol.*, 1914, p. 63.

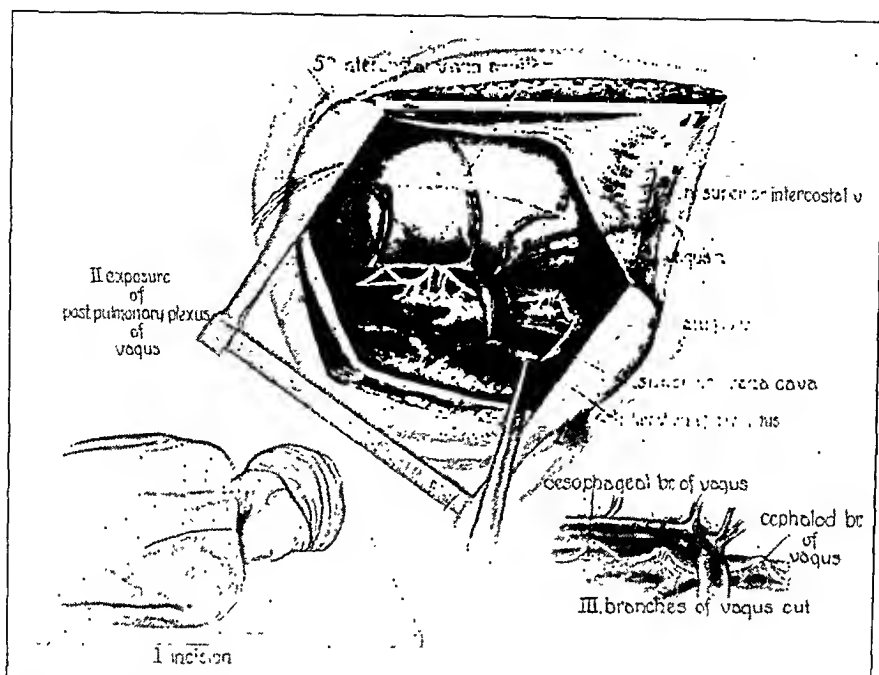


Fig. 1.—Resection of the posterior pulmonary plexus on the right side, showing incision and exposure of the posterior aspect of the hilus of the right lung.

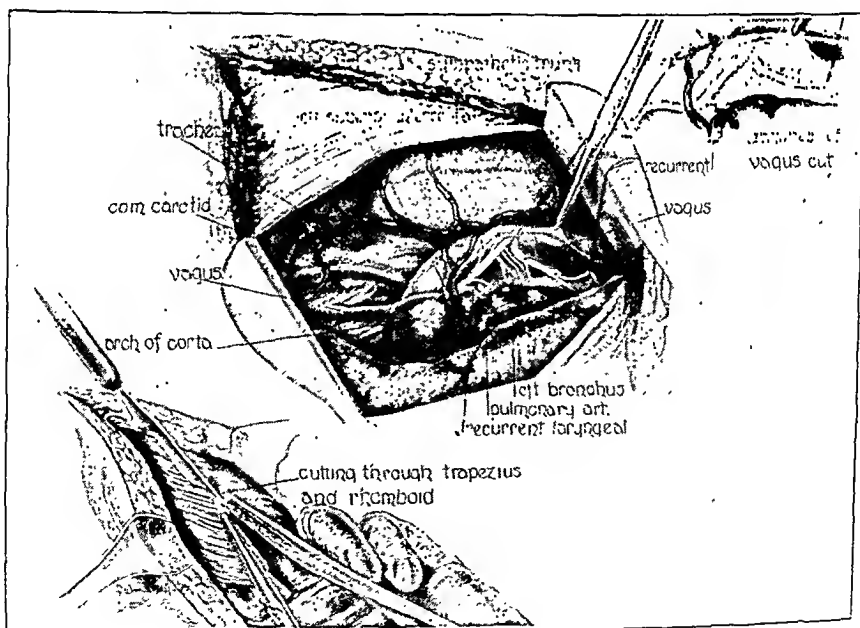


Fig. 2.—Resection of the posterior pulmonary plexus on the left side. The incision is carried down through the skin into muscle. Note the exposure of the vagus nerve and the posterior aspect of the hilus of the left lung.

is applied. This is removed with alcohol; the operative field is isolated in the usual manner by proper draping, and an incision is made in the interscapular region. The incision is begun on a level with the spinous process of the first thoracic vertebra, about 8 cm. below the upper border of the trapezius muscle and approximately 6 cm. lateral to the midline. It is continued downward and somewhat laterally to just below the angle of the scapula. The concavity of the incision faces lateralward and is in a general way parallel to the vertebral border of the scapula. The incision is similar to that used in the operation of posterior thoracoplasty but is not quite as long. The skin and subcutaneous tissue having been divided, the fascia covering the trapezius muscle is incised, and the fibers of the latter are divided directly over the fourth interspace on the right side and over the fifth on the left. In a similar manner the fibers of the rhomboid major muscle are also cut across. The incision is then continued down through the intercostal muscles, midway between the corresponding ribs so as to avoid the intercostal vessels and nerve. The pleural cavity is opened, and a self-retaining retractor is placed between the ribs in order to separate these sufficiently to expose the posterior surface of the hilus of the lung. As a rule, an intercostal incision of approximately 12 cm. will give sufficient exposure. It is true that the ribs are more closely approximated posteriorly, but even so they may be sufficiently separated. If not, one rib may be divided by means of rib shears. It has not been found necessary to resect a rib. In only a small percentage of cases have adhesions between the visceral and the parietal pleura been present, and such adhesions have always been easily dissected apart. Once the pleural cavity is opened, the posterior surface of the primary bronchi is exposed. A slight anatomic difference exists on the two sides. On the right side it has been found helpful to locate primarily the azygos vein, immediately inferior to which may be found the right primary bronchus. The vagus nerve is then discovered by incising the mediastinal pleura just cephalad to the azygos vein. It is important to locate the nerve at this point, for either just above or at the same level as the vein (or not infrequently even directly posterior) a rather large branch departs from the vagus and runs along the upper posterior border of the right pulmonary artery. The right vagus is then further exposed and mobilized from above the azygos vein in the posterior part of the mediastinum to a point below that at which the branches to the esophageal plexus depart. This point is well below or caudal to the hilus of the lung, but these branches to the esophageal plexus should be divided. The fibers running from the vagus and sympathetic trunks to the homolateral lung and the contralateral lung are thus readily and easily exposed, so that resection of at least 1 cm. of each of the nerve fibers may be accomplished. It is of the utmost importance to sever all of the branches of the posterior

pulmonary plexus not only to the same side but to the opposite side, for, as will be pointed out, this plexus contains the bronchoconstrictor fibers of both the vagus and the sympathetic trunk. The main trunk of the vagus should be handled as delicately as possible, so as to produce the minimum amount of trauma and therefore the least interference with function. For the sake of thoroughness it has become our custom to remove all areolar tissue from and around the bronchi and vessels in order to divide any unnoticed fibers which might course directly to or from the sympathetic trunk. In this manner the lung may be completely denervated. By elevation of the intratracheal pressure to 15 mm. of mercury the lung may be reexpanded and the air forced out of the pleural cavity. The ribs are then reapproximated with pericostal sutures of braided silk, and the muscles and fascia are sutured with interrupted stitches of fine silk. The skin is closed with interrupted fine silk sutures.

After two weeks the procedure is repeated on the left side, the only difference being that better exposure of the posterior surface of the hilus may be obtained by placing the intercostal incision one interspace lower on the left side, that is, in the fifth interspace. The vagus trunk will be found coursing over the transverse arch of the thoracic aorta, and the departure of the left recurrent or inferior laryngeal nerve may be observed just under the arch. The main trunk of the left vagus from this point down to that at which the first branch to the esophageal plexus is given off should then be freely mobilized and the fibers entering into the formation of the posterior pulmonary plexus exposed. As has been stated, resection rather than simple division of this plexus must be carried out, not only on the fibers running to the same side but also on those running to the contralateral side. The inferior or recurrent laryngeal nerve should be carefully avoided, for handling or even slight traction on this branch will produce temporary paralysis of the left vocal cord, resulting not only in transient aphonia but in some difficulties of breathing and deglutition. Such a complication produces an unfavorable psychic effect on the patient. In other respects the operative technic for the two sides is identical. The operation may be performed in a short time with no loss of blood, and in our series of cases it has been unattended by shock. There have been no postoperative complications after the procedure. The anesthetic employed has been either nitrous oxide and oxygen or cyclopropane, and a tight-fitting mask rather than an intratracheal tube has been used. Two-tenths gram of sodium amytal or pentobarbital sodium has been administered by mouth on the night and early morning preceding the operation. There have been no respiratory complications. In 3 cases after primary denervation of the left lung the right vagus trunk was divided deep in the neck, just below the point at which the recurrent laryngeal nerve is given off. After this procedure there was abdominal distention, lasting from forty-eight to

ninety-six hours, which was attributed to interference with the left vagus trunk as a result of handling. There was also, of course, complete loss of function of the right vagus caused by section. This type of procedure on the right side is not comparable to resection of the posterior pulmonary plexus from the standpoint of thorough denervation of the lung, because bronchoconstrictor fibers from the right vagus are given off high in the neck and course down the right sympathetic trunk; in the region of the second and third thoracic sympathetic ganglions they leave this trunk and join the posterior pulmonary plexus. With our patients, although there has been marked improvement as to both the frequency and the severity of the asthmatic attacks, there has been some persistence of mild and infrequent attacks. In the near future complete denervation of the right lung will be performed in such cases with the hope of completely eliminating the attacks. Procedures falling short of complete denervation of the lung by bilateral resection of the posterior pulmonary plexus are inadequate.

POSTOPERATIVE COURSE

Generally speaking, in all cases in which bilateral resection of the posterior pulmonary plexus has been performed the postoperative convalescence has been uneventful. The following exception should be noted: One patient, an elderly Negro, died several weeks after the second stage had been completed. The patient had suffered for years from asthmatic seizures associated with a high degree of arteriosclerosis, hypertension and some chronic myocardial change. He died suddenly after a cerebral hemorrhage unassociated in any way with the operation and after his asthmatic attacks had disappeared completely. Nothing abnormal was discovered in the heart, the lungs or the pleural cavity at autopsy. For the remaining patients the postoperative course was remarkably uniform, almost stereotyped. After the effects of the anesthetic had worn off following the completion of the first stage, the patient still had attacks of asthma. These attacks occurred almost as frequently as before but were far less severe, and much less epinephrine was required to bring about a subsidence of the seizure. One $\frac{1}{100}$ grain (0.6 mg.) of atropine would always bring about amelioration of an attack after the completion of the first stage of the operation. This has been considered of definite significance because of the well known paralyzing effect of atropine on the vagus nerve. In a larger series of cases the beneficial preoperative effects of atropine may furnish data that will prove helpful in selecting for operation only those patients with whom the condition is primarily neurogenic. On physical examination after the completion of the first stage it was discovered that most of the signs of bronchoconstriction were confined to the side of the chest on which no operation had been performed, and that probably

the sibilant, piping and squeaking rales audible on the surgically treated side were transmitted. A partial pneumothorax as a contributing factor in the production of these phenomena was excluded by a roentgenogram of the chest. During these unilateral asthmatic attacks the production of sputum was definitely reduced. No disturbance of respiration, either in rate or in rhythm, could be observed. After the second operation the frequency of the asthmatic attacks was generally much less, and there was an even more pronounced reduction in the severity of the attacks and their duration. In some patients the attacks ceased entirely. In the early weeks of convalescence the amount of sputum expelled was scanty compared to the copious amount produced before operation. One of the most striking results of the denervation was the disappearance of emphysema, which was present preoperatively in all cases. This was determined primarily by auscultatory findings and also by roentgenograms. The depth of respiration was greater after operation, while the rate decreased. In other words, the patients' respiratory mechanism more nearly approximated the normal. Unquestionably a great deal of the inspiratory and expiratory stridor caused by spasm of the bronchoconstrictor muscles as well as by excessive secretion of the bronchial glands could be explained on the basis of previous overactivity of the vagus nerve. Likewise, interference with the function of the vagi would relieve the patient of these difficulties provided such an aberrance of function were the underlying cause. This sequence of events, therefore, would seem to suggest that in the type of case dealt with in this series overactivity of the autonomic nervous system and particularly of the vagi played the major role in producing the attacks of paroxysmal respiratory dyspnea termed asthma. That there may have been some other factor or factors, such as infection or allergy, which furnished the immediate cause of the attack cannot be gainsaid in our present state of knowledge, but that removal of the influence of the extrinsic nerves was greatly beneficial in the majority of our cases and curative in some cannot be denied.

LATE RESULTS

A continuous follow-up study of these cases has been carried out, and for certain patients the postoperative convalescence as well as the subsequent clinical course has varied to some extent. These variations are noted here to emphasize the complexity and multiplicity of the factors producing such paroxysmal attacks of respiratory distress and to suggest that although the original causative factor has been removed, nevertheless in some cases in which the condition is of long standing the pathologic sequelae of these attacks may of themselves produce paroxysmal respiratory disturbances similar to the original asthmatic injuries.

Of the 10 patients discharged from the hospital, 1 was entirely unimproved; 1 improved for three months, finally succumbing to what seemed to be cardiac failure (this case will be discussed at greater length); 4 are completely well at the time of writing, having been free of attacks since operation or a short time later, and are able to resume their former work; 4 have occasional mild attacks of asthma, all of which are amenable to control by means of small doses of ephedrine.

The patient in whose condition there was no improvement after the operation was a poorly nourished Negro aged 56. He had chronic syphilis. He had been given antisiphilitic treatment for some time, but in spite of this aortitis had developed, resulting in insufficiency of the aortic valves. Whether or not this condition had any bearing on the continuation of his attacks of respiratory difficulty after operation is debatable, but it is at least within the realm of possibility that attacks of bronchial asthma superimposed on preexisting damage to the heart might have such a deleterious effect on the cardiac mechanism and consequently on the pulmonary circulation as to cause attacks of paroxysmal dyspnea almost indistinguishable from true bronchial asthma. However, the result in this case must be considered complete failure.

The second patient in whose case therapy failed was an engineer, referred to us by Dr. M. B. Cohen of Cleveland. The patient had been completely incapacitated before operation. His preoperative condition was almost one of status asthmaticus; he was confined, of course, to his bed and was forced to remain in the sitting posture practically the entire twenty-four hours. He had been studied most carefully in several clinics, and the condition was found to be unamenable to all forms of medicinal therapy. In spite of large doses of epinephrine administered daily for a number of years, the clinical course of his asthma had been continuously more severe. A copious amount of sputum was coughed up in the twenty-four hours, and there was pronounced emphysema. The patient was operated on, the posterior pulmonary plexus of one side being resected. After this procedure the asthmatic attacks were greatly reduced in severity as well as in frequency, and the amount of sputum was definitely diminished. For the first time the patient could sleep in the recumbent posture, and breathing was without effort. One afternoon the patient was asleep, breathing easily and normally. He was awakened by one of us, who talked on general subjects for some time. There was no disturbance in the respirations of the patient until he was informed that operation would be performed on the other side the next morning. In less than five minutes he was seized with a severe attack of asthma. After completion of the second stage of the operation, the patient was much improved for three months, during which time he was up and about and was considering a return to work. The sputum was reduced in amount, and the emphysema disappeared almost entirely. However, after three months paroxysmal attacks of respiratory distress recurred and the patient succumbed some months later to what appeared to be cardiac failure.

The interesting points to be noted in this case would seem to be: (1) the psychogenic factor in production of an attack, observed between the first and the second operation; (2) the prompt and pronounced reduction in the amount of sputum and the striking disappearance of the emphysema, suggesting that overactivity of the vagi played a major

role in the production of these respiratory attacks; and (3) relief from the asthmatic attacks for a period of three months, followed by eventual death from myocardial insufficiency, suggesting at least the possibility that the terminal attack of respiratory difficulty might have been partly or even entirely due to congestive cardiac failure. Thus a terminal pathologic condition probably produced by asthmatic attacks arising from another and specific cause might in itself be responsible for a continuation of these clinically similar seizures. It is not at all impossible that in a patient who is afflicted with a reactive or labile psychic and autonomic nervous system secondary pathologic changes can be indirectly produced, which may eventually prove fatal. Frequent examples of this may be cited: Raynaud's disease; instances of fatal angina pectoris; so-called neurogenic bronchial asthma; and anaphylactic shock. Smooth muscle spasm, as noted in an entire finger which is blanched from angiospasm as in Raynaud's disease, would have a different effect if the left coronary artery were involved or if the smooth bronchial musculature were affected.

Of the 4 patients who are completely well at the time of writing, only 2 were relieved at once after the operation on the second side. The remaining 2 were much improved immediately after the surgical resection of the posterior pulmonary plexus, but several months intervened before complete disappearance of the attacks. With the remaining 4, whose condition is vastly improved but who cannot be classified as completely well, this delayed or gradual disappearance of the asthmatic seizures may be taking place, and eventually they may entirely recover from the attacks.

COMMENT

The rationale of the operative resection of the posterior pulmonary plexus is based on the fact that the extrinsic nerve supply of the lungs consists of two entirely independent tracts, which have been demonstrated by dissection.² These tracts on account of their anatomic location and course have been termed the vagus, or bulbar motor lung, tract and the sympathetic, or spinal motor lung, tract, respectively. The preganglionic bulbar bronchomotor fibers arise in the dorsal vagus nucleus. From this point of origin they run in the vagus nerve trunk without interruption through the cervical and thoracic portions until they reach the region of the hilus of the lung. At this point they depart from the main trunk of the vagus by numerous small branches, mainly to the same but also to the opposite side or lung. Thus these branches form a part of the posterior pulmonary plexus on either side and end in the ganglions situated along the posterior surface of the main or

2. Møllgaard, H.: Studien über das respiratorische Nervensystem bei den Wirbeltieren, Skandinav. Arch. f. Physiol. 26:315, 1912.

primary bronchi. From these ganglions the postganglionic fibers are distributed through the lung to the bronchial musculature. In addition, the vagus nerve forms anastomoses with that of the opposite side not only in the cervical region but also directly beneath the root of the lung, as well as in the esophageal plexus. Once the fibers from the parent trunk have entered that of the opposite side, the greater number of them pass upward and are distributed to the lung of the corresponding side and that of the opposite side. Chiefly, the fibers between the vagi pass over in the first anastomosis.

According to all physiologic observations, the vagus in the human lung carries or contains mainly bronchoconstrictor nerve fibers. In certain animals, particularly the cat, the vagus carries bronchodilator as well as bronchoconstrictor fibers, but even in this animal the latter predominate. Stimulation of the distal end of the cut vagus in man and in animals produces bronchoconstriction of the same side and to a less extent of the opposite side. In addition to the anatomic proof, therefore, there is physiologic evidence of the crossed or bilateral innervation of the lungs through the vagi.

As shown by Iwama³ in experiments on the cat, the vagus nerve gives off in the cervical region anastomosing fibers to the sympathetic trunk of the same and the contralateral side. In the trunk these fibers course superiorly as well as inferiorly, so that both the right and the left sympathetic trunk in the neck and chest contain nerve fibers from the right as well as the left vagus nerve trunk. In the same manner sympathetic nerve fibers from the cervical sympathetic trunks of the same and the contralateral side are distributed to the vagi. Thus the vagus and sympathetic nerve trunks are composed of not only sympathetic but also parasympathetic nerve fibers.

The peripheral dissemination of the spinal fibers which run in the sympathetic trunk is not clearly known. In fact, there is no morphologic evidence of a spinal bronchomotor tract, but the results of physiologic experiments make it impossible to doubt the existence of such a tract. From the foregoing description of the frequent anastomoses between the vagus and the sympathetic trunk in both their cervical and their thoracic portions it is at once evident that not only in man but in animals used for experimental purposes, that is, the dog and the cat, there exists a vagosympathetic trunk; therefore, the possibility of the error of stimulating the parasympathetic trunk is evident. Although to a less extent compared to the vagi, the sympathetic fibers make a

3. Iwama, Y.: Untersuchung über die periphere Bahn des Nervus vagus: I. Die markhaltigen Fasern des rechten Vagus, *Folia anat. japon.* 3:215, 1925; II. Ueber den gegenseitigen Austausch der markhaltigen Nervenfasern der beiderseitigen Vagi am Brustteil, *ibid.* 3:281, 1925; III. Die markhaltigen Fasern des linken Vagus, *ibid.* 6:129, 1928.

definite contribution to the formation of the posterior pulmonary plexus. Unquestionably, afferent as well as efferent fibers are contained in these nerves running between the sympathetic trunks and the posterior pulmonary plexuses. There are probably sensory fibers accompanying the bronchomotor fibers in the vagus nerve also, but just as the bronchoconstrictor fibers predominate in the vagus, it seems likely that the sensory and bronchodilator fibers course mainly in the sympathetic trunk. The cells of origin of the vagus sensory tract, as is well known, lie in the ganglion nodosum, to which run fibers from the trachea and the lungs. Stimulation of the central trunk of the cut vagus or the intact vagus incites reflex narrowing or constriction of the bronchi.

Møllgaard² has shown that in the second and third thoracic spinal sympathetic ganglions lie cells which apparently send off sensory fibers to the lungs. Central stimulation of the superior cardiac nerve, the ansa of Vieussens or the superior thoracic nerve also produces bronchial constriction.

From these anatomic as well as physiologic observations, it seems logical to state that there is a dual nerve supply to each lung, the anatomic course of which is through the vagus and also through the sympathetic trunks. The preponderance of the fibers is to be found in the vagi, which undoubtedly supply mainly the bronchoconstrictor fibers to the lung of the same side and that of the opposite side. Owing to frequent anastomoses with the sympathetic trunks, it seems likely that these carry similar fibers. The presence of bronchodilator fibers in the human being has not been proved, but if they are present they would seem to be much overshadowed by the constrictor fibers. The theory that the action of the sympathetic and that of the vagal fibers are antagonistic is also without foundation. That both trunks carry sensory fibers has been definitely shown, and that the majority run in the vagus trunk would seem to be firmly established.

Dysfunction or imbalance of this autonomic nervous system, although poorly understood, is now generally recognized as a generic term which covers a multitude of clinical manifestations, depending entirely on the organ or organs innervated by the two extrinsic nervous systems. It would seem that this disturbance of the normally evenly balanced action of the sympathetic and parasympathetic systems may be localized to one or more organs and may or may not affect the entire body. There is an abundance of clinical evidence to support this statement, that is (1) Raynaud's disease, in which the arterioles of the hands and feet are chiefly affected; (2) the various forms of functional cardiac arrhythmia, such as paroxysmal tachycardia and premature systoles; (3) a small group of cases of essential hypertension; (4) ? diffuse goiter with severe hyperthyroidism, or exophthalmic goiter; (5) probably

some forms of migraine and minor cephalalgia, (6) many disturbances of the gastrointestinal tract, varying from cardiospasm, pylorospasm and spastic colon to Hirschsprung's disease; and (7) local dysfunction of the ureters and the bladder. All of these are but a few examples of pathologic disturbances which are either transient or prolonged evidence of an embarrassment or inequality of the normally symphonious action of these two antagonistic components of the vegetative nervous system. The lungs or the upper portion of the respiratory tract may be the site of this form of disturbed innervation. The clinical signs and symptoms evolved depend, of course, on the function of the organ or tissues so innervated and on the type of patient afflicted. As a rule, the psychobiologic reaction of the patient is far more labile than normal. There is, therefore, a psychogenic factor to be dealt with in all such cases of imbalance of the autonomic nervous system.

There are, as every experienced clinician is well aware, many cases of coryza, rhinorrhea, sneezing, nocturnal choking spells, globus hystericus, atypical hay fever, various forms of hyperpnea, even dyspnea and finally attacks of so-called nervous or neurogenic asthma in which the pathologic condition is unquestionably due to functional disturbances of the autonomic nerve supply to a part or the whole of the respiratory tract and is not based on, but may be associated with, an allergic reaction or infection. It was to patients suffering from almost continuous attacks of asthma or status asthmaticus and totally incapacitated as a result of this malady that our attention was directed. After a long period of study and treatment in the asthma clinic of the Johns Hopkins Hospital, this condition has been given up as hopeless from the standpoint of medicinal therapy and referred for surgical treatment as a last resort. It is felt desirable to report this actually small but relatively large group of cases at this time because about four years has now elapsed since the first operation was performed. Unquestionably there are many causes of bronchial asthma, and, as would be expected, the literature on this subject is voluminous. One of the most outstanding monographs is that of Alexander, which affords a detailed discussion of the causes and effects of this malady. It seems likely that the mechanism involved in the production of an asthmatic attack is unquestionably a narrowing of the bronchial tube with a subsequent increase in the resistance to the free inflow and outflow of air. This state of stagnation of ventilation indirectly produces changes in the blood gases and results in dyspnea of a greater or lesser degree, depending on the extent of occlusion of the bronchial tree. This occlusion may be considered as largely and in its simplest terms due to: first, spasm of the bronchoconstriction muscles; second, edematous swelling of the mucous membranes of the smaller bronchioles; third, increase in the amount and viscosity of the

secretion of the bronchial glands. In all instances of bronchial asthmatic attacks the three aforementioned factors probably play a major role, in spite of the additional etiologic factor or factors which may be involved in the production of such attacks. In many cases the asthmatic attacks can be explained directly on an allergic basis or indirectly on an infectious one. In some, however, when the former two causes have been eliminated the attacks can be ascribed only to a disturbance in the function of the autonomic or extrinsic nerve supply to the lung. The resultant effect on the bronchoconstrictor muscles, as well as the increased activity of the mucous membrane with its concomitant edema, and also the altered character and increased amount of the bronchial secretion produce a narrowing of the airways, causing associated dyspnea and other physical symptoms. The mechanism of production of an asthmatic seizure may be at least markedly influenced by the extrinsic nerve supply to the lung.

Doubtless in the majority of cases an important psychogenic factor is associated with a definite imbalance in the extrinsic nerve supply to the lungs. Along with this rather labile psychoneurogenic mechanism there may or may not be present a concomitant allergic or infectious element that plays a role of greater or less importance in the precipitation of attacks of asthma. In all probability such attacks of paroxysmal dyspnea associated with generalized bronchoconstriction and bronchorrhea and called asthmatic attacks are caused by many different etiologic factors. In some the psychoneurogenic element predominates, while in others infection or allergy plays the major role. In all, however, there is a large nervous element. The discovery of an allergic basis for attacks of bronchial asthma and their relief by medicinal measures form one of the most brilliant advances in therapeutic knowledge in the last few decades. However, although large, the group of patients with allergic asthma is far from all-inclusive, excluding as it were all of those persons in whom the psychoneurogenic or infectious element or both might be considered causative. Unfortunately for the latter patients, numerous different forms of therapeutic measures have been resorted to, and in spite of medicinal treatment the attacks continue unabated.

After medicinal methods had been exhausted in a futile attempt to alleviate the attacks for this most unfortunate group of patients, other forms of therapy were resorted to, such as high voltage roentgen therapy, injection of alcohol into the sympathetic trunk on one side and numerous operative procedures. For an excellent review of the many and bizarre operations which have been devised, performed and evaluated from the postoperative results, the splendid article by Phillips and

Scott⁴ should be referred to. The failure of surgical treatment in the majority of cases of bronchial asthma in the past as well as the mediocre results obtained in the remainder, or minority, of cases may, it would appear, be attributed to the fact that the operations have been entirely inadequate. In some only the sympathetic trunk on one side has been severed; in others only one vagus trunk has been severed; in a very few a unilateral excision of the posterior pulmonary plexus has been performed. The course of the fibers composing the posterior pulmonary plexus makes it mandatory to perform a meticulous bilateral resection of the latter in order to isolate the lung completely from its extrinsic nerve supply. Any procedure short of this will be inadequate. It necessarily follows that the postoperative results will correspond directly to the degree of completeness with which the operation is carried out. The posterior aspect of the hilus is the only point at which all the efferent and afferent fibers composing the extrinsic nerve supply to the lung can be interrupted. It seems likely that because of this fact the operative results in the series of cases reported on here have been better than any of those reported in the past.

The ideal result, that is, complete cure, will of course be confined to cases in which the attacks of asthma are entirely psychoneurogenic and are not of many years' duration. An operation of this type can relieve only bronchoconstriction, edema of the mucosa and bronchorrhea which is vagal in origin. The greater the role played by allergy or infection, the greater the departure will be from this ideal result. On the other hand, even if a complete cure cannot be obtained, relief in varying degrees may be given. This not only will result in an infinitely more comfortable life for the patient and make it possible for him to return to work, but (a fact of greater importance) may remove the strain from an already overtaxed heart. When secondary pathologic changes have been wrought over a period of years and irreparable damage has been done to the heart muscle, attacks of paroxysmal dyspnea, cardiac in origin, may supervene even though the true asthmatic seizures have disappeared or have been very much subdued. When this occurs, the patient, as a rule, dies from circulatory failure of the pulmonary system, due in the main to myocardial weakness. For these reasons careful cardiovascular surveys should be made before a patient afflicted with paroxysmal attacks of dyspnea is subjected to an operative procedure of this type. On the other hand, a patient incapacitated from asthmatic attacks of unknown cause should be so operated on, not only because the operation may restore him to normal health but also because it may at least alleviate the attacks sufficiently to prevent further damage to the cardiovascular system.

4. Phillips, E. W., and Scott, W. J.: Surgical Treatment of Bronchial Asthma, *Arch. Surg.* 19:1425 (Dec., pt. 2) 1929.

BEHAVIOR OF JOINT CARTILAGE IN LATE RICKETS

CONTRIBUTION TO THE QUESTION OF ATROPHY OF CARTILAGE

ERNST FREUND, M.D.

LOS ANGELES

Considerable work has been done to clarify the morphologic changes of the zones of enchondral growth in patients with rickets, and hardly anything new can be added. However, investigators doing such work have paid little attention to the behavior of joint cartilage, although one might think that a number of biologic questions concerning joint cartilage might be answered by such study. I mean, especially, the still debated question of the importance of enchondral ossification of joint cartilage for the growth of the epiphyses, and also the question whether simple atrophy of cartilage may occur. It is clear that simple rickets as it occurs in earliest childhood can hardly be of use for the study of joint cartilage, because the cartilage has not fully developed; the thick cartilage cap still completely surrounds the bony epiphysis. On the other hand, reports of careful anatomic examinations of patients with late rickets, in whom the joint cartilage is of more mature development, are rare; and even the best works on the subject, by Looser¹ and by Schmorl,² do not mention changes in the joint cartilages. I recently finished an article³ on the roentgenologic and histologic changes observed in 3 cases of severe late rickets, and I have observed certain alterations in the joint cartilages which I consider worthy of separate mention.

I shall first give a short report on the 3 cases in which the condition was observed at autopsy during the World War, collected at the City Hospital of Vienna.

CASE 1.—A 15 year old girl had extreme deformities of all the extremities. The body length was only 87 cm. The patient had had rickets from childhood and had never walked. She had never attended school and was mentally retarded. She had scorbutic bloody suffusions of the lower extremities and gingivitis suppurativa with gangrene of the lower lip and the gum.

CASE 2.—A 22 year old woman of infantile habitus had gummatous osteoperiostitis of the skull and also syphilitic saddle nose. The body length was 142 cm.

From the Orthopedic Department, College of Medical Evangelists.

1. Looser, E.: *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **18**:678, 1908; *Deutsche Ztschr. f. Chir.* **152**:210, 1920.

2. Schmorl, G.: *Deutsches Arch. f. klin. Med.* **85**:174, 1905.

3. Freund, E.: On Three Cases of Late Rickets, *Am. J. Roentgenol.*, to be published.

There were severe rachitic deformities of the spine and the extremities. Scurvy was present. The patient died of Spanish influenza.

CASE 3.—A 25 year old woman, an imbecile, underdeveloped and of infantile habitus, 126 cm. in body length, was supposedly normal until the age of 14. Late rickets was present; the patient could not sit or walk. Death was caused by pulmonary tuberculosis.

It is questionable whether one may expect to find specific rachitic changes in the joint cartilages. It is well known that the degree of alteration of cartilage in rickets depends on the inherent rapidity of enchondral ossification, which varies with different parts of the body. This explains the fact that a patient in whom considerable changes are observable at the costochondral junction may have no signs of rickets at a slowly growing epiphysial plate, for instance, the lower end of the humerus. It is well known, further, that rachitic changes appear only at the diaphysial side of the cartilage plate, which is the site of enchondral ossification, while the epiphysial side, owing to the inactivity of enchondral ossification, usually presents no rachitic signs. As far as enchondral ossification is concerned, the joint cartilage behaves similarly in many ways to the epiphysial side of the cartilage plate, which means that it presents little activity; and for this reason alone one must be prepared for failure to discover rachitic changes in the joint cartilage. However, it is logical to conclude that the enchondral ossification of joint cartilage represents the only possibility of enlargement of the bony portion of the epiphysis, and severe rickets, which leaves its marks on all the epiphysial plates of the body—and in most of the cases of late rickets observed during the war the condition was severe—will hardly leave the joint cartilage unaltered.

As a matter of fact, in the various joints which I examined I observed pictures which varied from the approximately normal, as in the elbow joints of the patient in case 1, to severe and unusual pathologic change, as in the knee joint of the patient in case 3. But even in the most severely affected joints the principal pathologic process could hardly be interpreted as rachitic; the changes were nonspecific and were due to atrophy. Even so, however, they were of considerable interest and were certainly related to the existing rachitic process.

The question has often been discussed whether joint cartilage, as a bradytrophic organ in which the number of cells once the cartilage has reached structural maturity remains more or less constant, can undergo atrophy, which means diminution of its cells, in the same way as other organs do.

SIMPLE ATROPHY OF JOINT CARTILAGE

Müller⁴ in his book on the biology of the joints, stated that even in the most advanced forms of bony atrophy the joint carti-

4. Müller, W.: *Biologie der Gelenke*, Leipzig, Johann Ambrosius Barth, 1929.

lages do not show changes in the number of cells. I, however, feel that the discussion about atrophy of cartilage is much ado about a pseudo-problem. There is no doubt that joint cartilage can undergo atrophy just as does the underlying bone, and any one who has examined a number of senile joints will confirm this. Pommer's idea that bony atrophy in its simplest form results from a prevalence of physiologic absorption of bone over apposition of bone can also be applied to joint cartilage. Joint cartilage under physiologic use shows constant wearing off of cells and ground substance at its superficial layers. To compensate for the loss, the cartilage cells or cell groups in the deeper layers and at the margins of the joint cartilage proliferate. Under normal circumstances such proliferation is not a very active process, and it is hardly recognizable microscopically in adults. Its existence has been denied by some investigators because of lack of histologic evidence, and a form of amitotic division of the superficial cartilage cells has been assumed to compensate for the wear. Be this as it may, atrophy of joint cartilage must ensue as soon as the compensatory proliferation fails to keep pace with the wearing off of the upper layer. Such atrophy occurs in association with many forms of degenerative arthritis or in cases in which there is absorption of joint cartilage under a fibrous tissue pannus. In such cases thinning of the joint cartilage occurs by resorption or loss of cartilage from above, and the result is atrophy of joint cartilage.

ATROPHY FROM DISUSE

Another characteristic form of cartilage atrophy is that caused by disuse. Joint cartilage needs function for its preservation. It will slowly disappear when it is put out of action. Absorption takes place from the margins of the joint and from the bone marrow, and especially at the marginal portions of the joint surface which have lost normal contact with the antagonistic end of the joint, as in articular contracture. I recently reported⁵ on the histologic changes of joint cartilage during infraphysiologic use and stressed their importance for the development of the final shape of the ends of the joint in cases in which disuse sets in at an early age. If disuse of a joint takes place in an adult, especially for extra-articular reasons, then the subchondral hard substances, the bony lamina and the calcified joint cartilage will disappear first, usually by osteoclastic absorption, and later a slow, smooth absorption of joint cartilage can be observed which may gradually lead to complete disappearance of the cartilage. Such pictures are not rare for paralyzed senile joints with or without deformity and especially in the proximal fragment in case of nonunion of fracture of the neck of the femur. In

5. Freund, E.: Joint Cartilage Under Infra-Ultra and Euphysiologic Demands. Arch. Surg., to be published.

all such cases the atrophy of the joint cartilage corresponds to the bony atrophy of the joint ends; it is only a concomitant symptom of skeletal atrophy.

The 3 patients with adult rickets mentioned in this paper showed atrophy of articular cartilage in both forms; there was absorption from above by a fibrous tissue pannus, but the thinning out of joint cartilage was principally caused by smooth absorption from below. Signs of enchondral ossification of the joint cartilage, which might have been expected in all the joints because of the presence of epiphysial plates in other regions of the body, were rarely seen in the more severely involved joints. Cartilage proliferation especially, which was so pronounced at the epiphysial plates even in the patients aged 22 and 25, in whom it had caused tumor-like accumulation of cartilage cells, was entirely absent in the joint cartilage. It is certain that rickets does not stimulate cartilage proliferation; so even the tumor-like chondromatous masses at the metaphysial sides represent only accumulation of cartilage tissue which has formed during many years of retarded or absent enchondral ossification. It is not a sign of overproduction of cartilage, but only a sign of the persisting proliferative phase of enchondral ossification (which, as a whole, is probably considerably slower than normal, in accordance with the retarded growth and the general hypoplasia of the rachitic patient) and of the complete absence of the phase of ossification due to the lack of cartilage calcification. A noticeable accumulation of cartilage cells cannot be expected at the articular cartilage, the growth of which is physiologically very slow and in which absorption at the lower surface can easily keep pace with proliferation.

ENCHONDRAL OSSIFICATION OF JOINT CARTILAGE

One must also consider the fact that during normal epiphysial growth there is always a reduction of the thickness of the cartilaginous cap of the bony epiphysis. The reduction takes place by slow enchondral ossification, which leads to the enlargement of the bony epiphysis. It is a well balanced process of proliferation and ossification of cartilage, the latter being slightly predominant. When epiphysial growth stops, the cartilage cap has been reduced to the normal thickness of joint cartilage. This means that thinning out of the cartilaginous cover of the bony epiphysis which occurs by means of normal absorption is a somewhat more rapid process than proliferation. Both processes are slowed down in cases of late rickets; proliferation of joint cartilage is at a complete standstill, but absorption from the marrow spaces continues. The result must be that the epiphysis does not show any increase in size, though the bony portion may be enlarged very slightly at the expense of the joint cartilage. The lack of proliferation of the joint cartilage is another proof of the fact that rickets does not stimulate growth of cartilage.

PHYSIOLOGIC NECROSIS OF CARTILAGE CELLS

The most frequent histologic changes observed (fig. 1) were the following: The joint cartilage appeared rather thin but was mostly smooth on the surface. It usually permitted an easy differentiation into 3 layers. The most superficial one, comprising approximately two fifths of the thickness, could be considered as a gliding layer with fusiform cells parallel to the joint surface. A good many of these cells were only shadows, necrotic, in the stage of "Verdämmerung" (Schaffer⁶); they contributed by their transformation to ground substance to the enlargement of the intercellular areas. This was a sign that the joint

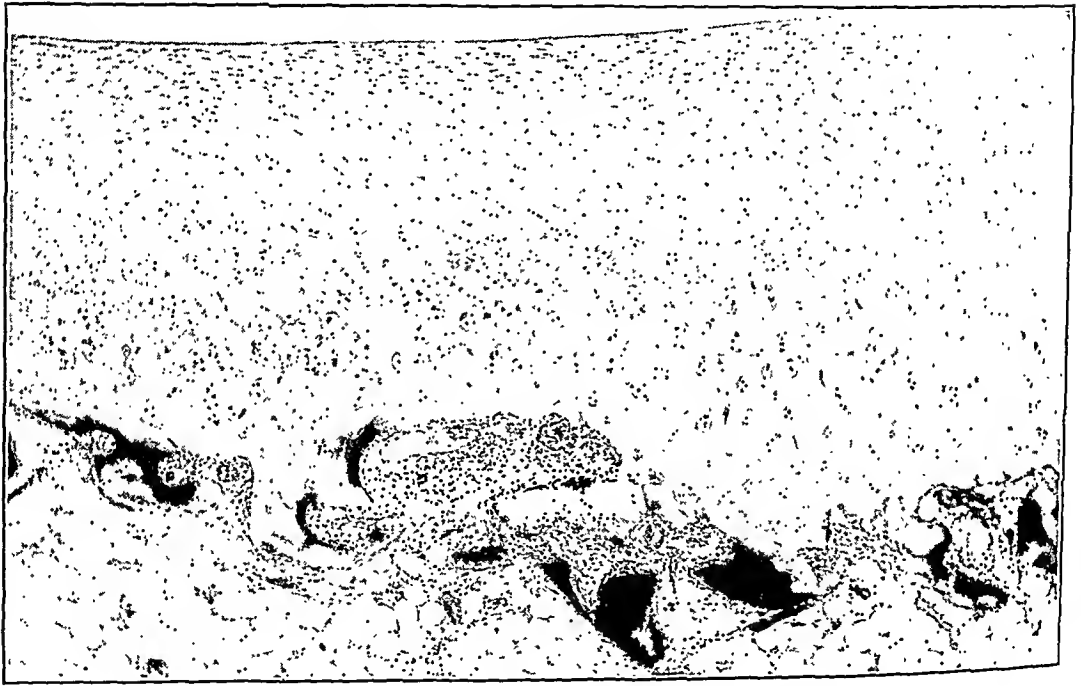


Fig. 1 (case 3).—Upper joint surface of the tibia, enlarged about 43 times, showing irregularity of the lower surface of the joint cartilage, which lacks a distinct zone of calcification and a subchondral bony lamina. There is a high degree of osteoporosis. Marrow spaces enter the noncalcified joint cartilage and replace it by fibrous tissue. The structure of the joint cartilage is immature. Enlargement of the cartilaginous cells has occurred in the lower half, with no increase of cellular proliferation. Note the infantile crisscross arrangement of cells in the upper half of the joint cartilage.

cartilage had not yet reached mature functional structure; in most joints it had remained in an infantile stage and the differentiation of its cells was deficient. The middle two fifths was characterized by relatively

6. Schaffer, J.: *Lehrbuch der Histologie und Histogenese*, ed. 3, Leipzig, Wilhelm Engelmann, 1933.

large cell cavities with proliferating cartilage cells, three to five in one cavity, with some clear bluish protoplasm which suggested the mucoid degeneration so frequently observed in older patients with degenerative cartilage proliferation. There were neither cell capsules nor pericellular halos; the hyaline ground substance lacked normal basophilia and bordered on the cell cavities without any tinctorial differences. It gave the impression of little consistency, which was suggestive of edema of the cartilage. The number of degenerating cells was greater in this region than in the superficial layers, and the relatively wide intercellular spaces permitted the discerning almost throughout of shadows of former cartilage cells. The edema of the middle layer of joint cartilage, which sometimes extended even into the superficial strata, made the cartilage appear of little mechanical resistance, which was contrary to a normal zone of passage between the superficial gliding layer and the deep pressure layer. The distribution of the cartilage cell groups was irregular; it was still more of the infantile crisscross arrangement and was far from being a functional structure with radial orientation of the cells, such as might have been expected from the relatively advanced age of the patients. The lowermost fifth was unusual. The cartilaginous ground substance in this region appeared darker and was evidently harder, and the cells formed small groups without proliferation and without elongation. This is remarkable because this deepest stratum of the pressure zone is usually during the years of skeletal growth the stratum showing the most active cellular proliferation. It is from this layer that replacement of the worn-off superficial cells takes place. Another surprising fact was that this layer was also the richest in necrotic cells. No special reason for this peculiar behavior could be discovered. It seemed, however, that although necrosis of cartilage cells and their transformation to hyaline ground substance are normal conditions in the period during which the joint cartilage acquires its mature functional structure, the number of necrotic cells in the joint cartilages studied was unusually high. It may be that nutritional deficiency accounted for it.

The manner in which the bone marrow bordered at the joint cartilage differed considerably from region to region. The patient in case 1, the youngest of the patients, showed a very irregular process of enchondral ossification with a deficient layer of calcification (fig. 2). Spots of calcified cartilage were sporadic and comprised only one layer of cartilage cells. There was no sharp line between the calcified and the uncalcified cartilage. Marrow spaces entered the cartilage with engorged vessels and ascended for a considerable distance into the noncalcified pressure layer (fig. 2). This was not according to a normal process of enchondral ossification; it rather resembled pictures of degenerative arthritis, of which Pommer considered the invasion of noncalcified cartilage by marrow spaces to be highly characteristic. In such cases it is the degenera-

tion of cartilage, especially the decrease in its elasticity, which fosters the invasion of marrow spaces as a reactive change from the side of bone marrow. It may be that similar alteration of the physical property of the articular cartilage takes place in cases of severe rickets, although the histologic evidence is relatively poor. However, the edema of hyaline ground substance and the frequent necrosis of cartilage cells suggest serious damage, to which the absorption by marrow spaces may be the direct response.

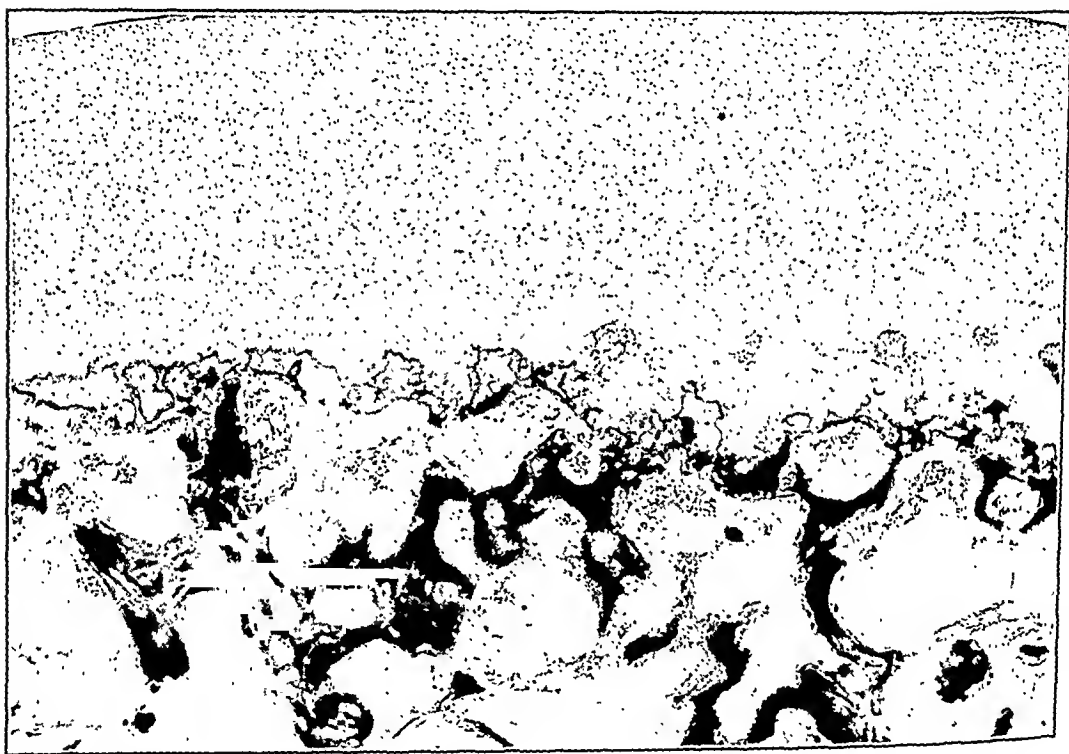


Fig. 2 (case 1).—Head of the femur of humerus, enlarged about 27 times. Note the typical rachitic changes in the subchondral zone and also the bony trabeculae, coarse and with wide osteoid layers. There is extensive osteoclastic bone absorption. The zone of calcification is irregular and is interrupted in many places by marrow spaces which deeply invade the noncalcified joint cartilage. The joint cartilage is without functional structure. There is beginning formation of intercellular territories in the lower half of the bone.

In these cases cartilage became absorbed by bone marrow along a fairly straight and sharp line more often than by small marrow spaces (figs. 3 and 8); it was a form of smooth absorption of the noncalcified cartilage after complete removal of the subchondral hard substances. Chondroclasts did not play an outstanding role in this form of absorp-

tion; they were rather rare, and the disappearance of cartilage, if it was a cellular process at all, was maintained by mononuclear fibrocytes. In both instances, whether there were smaller marrow spaces ascending far into the noncalcified cartilage or whether there were large marrow sinuses bordering directly on the lower surface of the cartilage, the result was the same; joint cartilage disappeared by a process of incomplete absorption and not by enchondral ossification. This means that the collagenous fibers of the cartilaginous ground substance persisted in part, and after their liberation from the hyaline cement substance helped



Fig. 3 (case 1).—Lower joint surface of the femur enlarged about 35 times. Note the smooth absorption of the joint cartilage from below and the formation of a subchondral zone of fibrous bone marrow and atrophic bony trabeculae. There is complete lack of a zone of calcification and of subchondral bony lamina. The structure of the articular cartilage is immature: there are no signs of cellular proliferation.

to form the subchondral bone marrow, which was typically loose fibrous tissue. It was possible in every instance to demonstrate how the fibrils of the bone marrow emerged directly into the hyaline ground substance, or, better, emerged from the cartilage and mingled with the fibers of the bone marrow. The joint cartilage disappeared without being replaced by bony tissue.

PERSISTENCE OF CARTILAGINOUS CELLS

The numerous marrow spaces along the lower surface of the joint cartilage often contained a number of isolated cartilage cells (fig. 4) or even smaller cell groups as they temporarily escaped the cartilage absorption. It seemed that the incomplete process of cartilage absorption often preserved not only the collagenous fibers which helped to form the subchondral fibrous bone marrow but also at least a part of the cartilage cells, which later, when the cell capsules had been dissolved, changed to fibrocytes and disappeared among the other cells of the bone marrow.

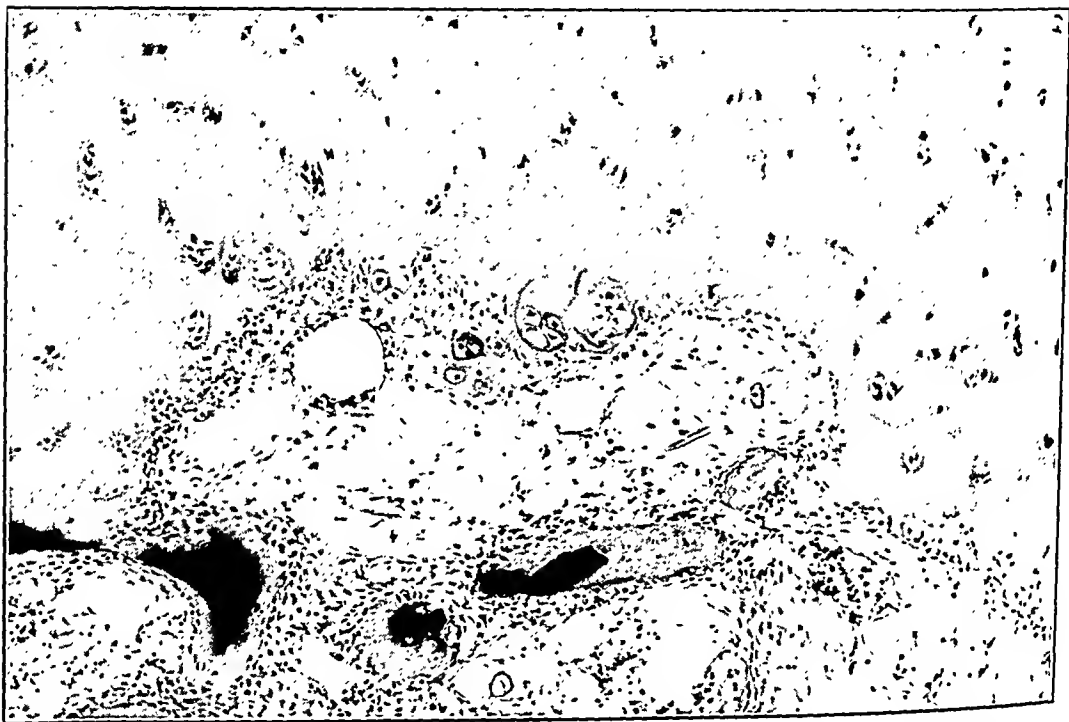


Fig. 4 (case 1).—Head of the femur, enlarged about 100 times. Note the incomplete absorption of the joint cartilage from below. Note also the loose fibrous bone marrow dissolving the hyaline intercellular ground substance. There is preservation of collagenous fibers and temporarily of cartilage cells and cell groups. The cartilage cells change to fibrocytes after the cell capsules have been dissolved. Note the wide osteoid layers of the bony trabeculae. Many cartilage cells in the stage of "*Verdämmerung*," merely shadows, add to the widening of the intercellular territories.

FILLINGS OF CARTILAGINOUS DEFECTS

Occasionally one noticed that some of the marrow spaces within the noncalcified cartilage had again become filled with a more primitive type of cartilage which certainly originated from the isolated cartilage cells (fig. 5). Such secondary "fillings" of marrow spaces are not unusual

in rib cartilages or in the hyaline cartilaginous plates of the intervertebral disk; they are also found in epiphysial plates and represent a change which is hard to classify as degenerative or reparative. They are extremely unusual in joint cartilages and were also rare in these cases of late rickets. Wherever they were observed the free surface of the joint cartilage was covered by a fibrous tissue pannus under which joint cartilage was absorbed along a rather sharp lacunar line, but with preservation of collagenous fibers and also of cartilage cells, which under proliferation changed to fibrocytes; that is, another process of incomplete cartilage absorption was taking place on the upper surface

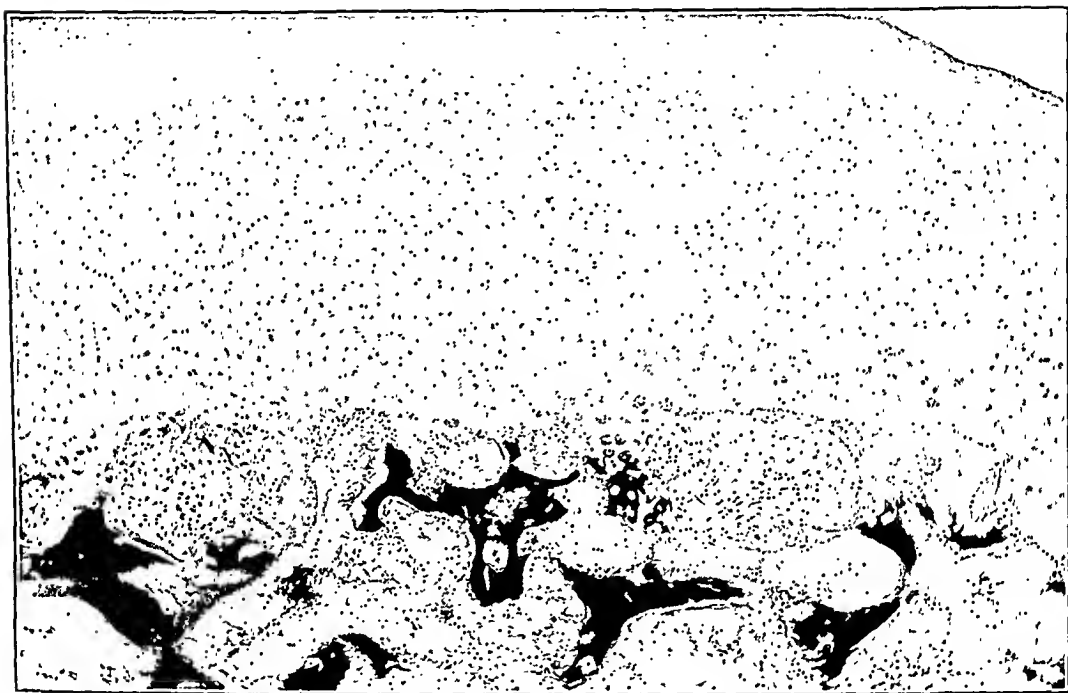


Fig. 5 (case 1).—Head of the femur, enlarged about 37 times. Note the filling of fibrous marrow spaces at the site of the joint cartilage by young proliferating cartilage tissue. Note also the typical rachitic changes of the subchondral bone and the primitive structure of the joint cartilage. There is beginning absorption of the superficial layers by an avascular fibrous tissue pannus. Most of the collagenous fibers derive from the hyaline cartilage itself, which by losing the hyaline chondromucoid cement substance exposes its collagenous fibers.

of the joint cartilage. The loss of cartilage on both surfaces, by a fibrous tissue pannus from above and by marrow spaces from below, suggests that the fillings of new cartilage at the lower surface represent a compensation for the thinning out of the joint cartilage from above. In all other places—and they are the majority—where there is only thinning from below, no attempt is made toward proliferation.

The loss of cartilage by absorption from below was one of the outstanding features in the behavior of joint cartilage in my 3 cases of late rickets. As a rule there was no cellular proliferation connected with this process. It had nothing to do with enchondral ossification; it was probably caused by an intrinsic physicochemical damage of the ground substance, by the inactivity of the joints, and as such it was a concomitant symptom of the severe atrophy of the skeleton. As has been mentioned, essentially the same type of atrophy of joint cartilage is frequently found in senile patients. For comparison I shall include an illustration of the broken head of a femur (fig. 6 and 7). The subchondral hard substances have disappeared almost entirely, and thickness

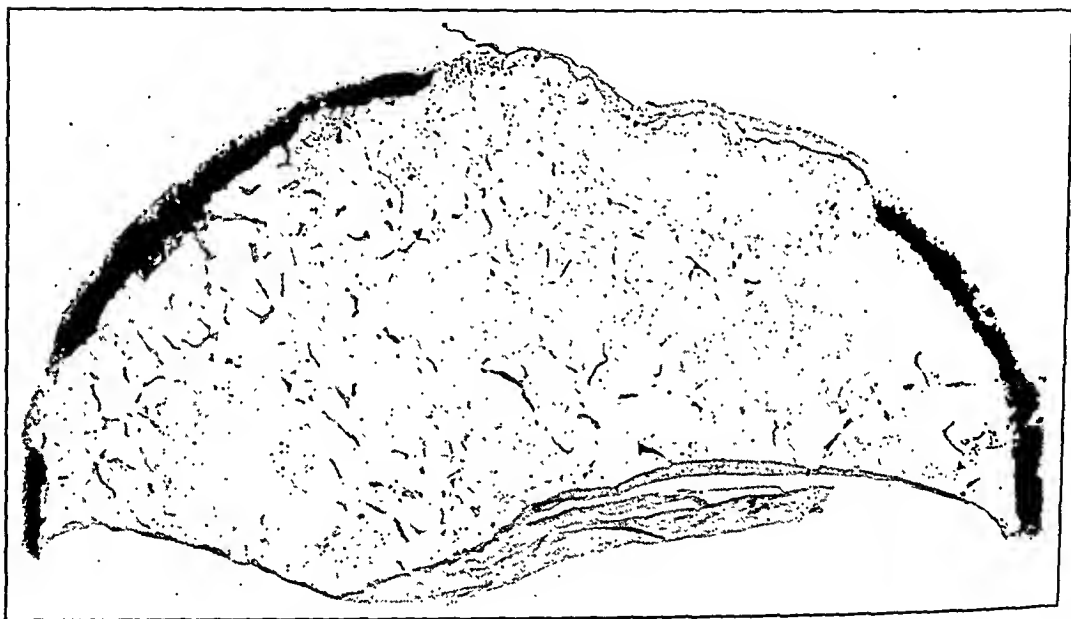


Fig. 6.—Broken head of the femur, without union, enlarged $3\frac{1}{3}$ times. There is extreme bony atrophy with thinning of degenerated cartilage, mainly by smooth absorption from below.

of the joint cartilage has been reduced to about half or even less by resorption from below. Thus far the picture is identical with that described for late rickets. It is, however, surprising to note how much proliferative activity the senile joint cartilage displays, while in cases of late rickets there seems to be not the least effort to compensate for the loss. Of course, it cannot be denied that the proliferation associated with senile atrophy may be solely degenerative; if so, it should not be considered as an attempt at regeneration. It frequently occurs in senile patients with degenerative arthritis without atrophic changes in the subchondral zone. Whether it is called degenerative or regenerative proliferation, however, its effect is that joint cartilage invaded severely

by absorption from below will remain intact for a much longer period than it would without cellular proliferation, and one still wonders why the joint cartilage in cases of late rickets yields so readily to absorption. Changes in the physicochemical properties are present with senile atrophy of cartilage as well as with late rickets: the two conditions have inactivity and bony atrophy in common; and as far as regeneration is concerned, the patient with rickets should certainly possess more than the senile patient. Again one is driven to the assumption of a more specific damage of joint cartilage by rickets, a form of paralysis of the tissue caused by the nutritional disorder. (The apparent proliferation of cartilage at the epiphysial plates does not speak against this assumption, because, first, the different cartilage tissues of the body lead individual existences: one may be more active than another: and



Fig. 7.—Same section as in figure 6, enlarged about 27 times. The zones of cartilage calcification and the subchondral bony lamina have disappeared almost entirely. There is smooth absorption of the cartilage by bone marrow. There is proliferation of cartilage cell groups with erosion and fibrillation of the superficial cartilage layer.

also it is most unlikely that the tumor-like enlargement of the epiphysial plates is caused by superactive cartilage proliferation. It may be merely the expression of the lack of absorption of cartilage which has existed for several years.)

I feel, however, that there is still another factor which should be considered. There is no doubt that normal joint cartilage goes through a hard training during its many years of existence. This finds its morphologic expression in a highly mature functional structure which varies with the different types of joint. The high structural differentiation of the articular cartilages is usually taken as the main reason for the

lack of cartilage regeneration. Lubosch maintained that the high specificity of joint cartilage prevents further progressive development. This is certainly true, but the statement should not be taken as absolute proof that joint cartilage has not the power to regenerate. Mature hyaline cartilage is unable to produce cartilage tissue of like maturity to repair defects or injuries. All the regenerative phases are preceded by a backward development, in which the type of cartilage cells changes first to that of the fibrocytes, and then by further proliferation to a more primitive (fibrous) cartilaginous tissue. This inherent power to proliferate frequently can be observed in joint cartilage after all kinds of injuries. It may become manifest in senile patients when degenerative changes take place in the intercellular ground substance. It is a typical feature of degenerative and hypertrophic arthritis. It explains the considerable proliferation of the joint cartilage in the otherwise porotic fractured head of the femur.

The general underdevelopment of these 3 patients with late rickets and the fact that the joints of the lower extremities in cases 2 and 3 were hardly ever weight bearing suggest that the articular cartilages lacked special functional training and were not fit for survival. There was not enough vital force even for degenerative proliferation. The joint cartilages remained entirely passive and yielded to the absorption from below.

Occasionally a more or less coherent stretch of bony trabeculae, parallel to the lower surface of joint cartilage, indicated its former lower level. An extensive part of the joint cartilage had disappeared, either by smooth absorption without formation of fibrous bone marrow in the subchondral zone or because of the presence of small marrow spaces which later became confluent.

DISSECTION OF JOINT CARTILAGE BY ABSORPTION

The absorption of joint cartilage from below was not seen in every case to attack the deepest cartilage layer exclusively. Marrow spaces could be seen extending to the sides within the noncalcified pressure layer of the joint cartilage, thus separating a strip of cartilage as if by dissection. Such strips, often in connection with atrophic bone, sometimes persisted for some time, thus giving a landmark which showed how much of noncalcified cartilage had already become absorbed under extension of the intracartilaginous marrow spaces. This was again a picture similar to that observed with hypertrophic arthritis, with which exostoses develop at the site of the joint cartilage. In this condition also the deepest layers of joint cartilage, especially the calcified layer, may often persist in tongue-like form while the exostosis forms above them by enchondral ossification of the joint cartilage. The main difference

between the two processes consists in the fact that in late rickets the joint cartilage is entirely passive and there is almost no osteogenesis at its previous site, while in hypertrophic arthritis it proliferates, thus causing displacement of the joint surface to a higher level. (Or, because the joint cavity represents only a fictitious space which does not permit the enlargement of the joint end toward or into the joint cavity, the convex joint end is gradually displaced from the articulation [subluxated] to the extent to which the joint ends enlarge by enchondral ossification of the cartilage.) One might feel especially on the basis of Pommer's investigations and interpretations, that the absorption of joint cartilage by bone marrow is a sign of arthritis deformans. However, this would signify an overemphasis of the histologic picture. I do not share Pommer's conviction that the invasion of noncalcified joint cartilage by marrow spaces is of pathognomonic importance; it occurs too often as an entirely nonspecific response of bone marrow to essentially different lesions of joint cartilage. Rather than with arthritis deformans (hypertrophic arthritis) I should correlate the smooth absorption of the articular cartilage in my cases to atrophic changes; the numerous small marrow spaces doubtless resulted from incomplete cartilage absorption in atrophic arthritis. In such cases, in subacute and chronic stages there are typically rather vascularized marrow spaces in the lower layers of the joint cartilage; as a rule, however, bone formation at the former site of the joint cartilage does not ensue. This means that the similarity of the histologic pictures is merely external. In cases of atrophic arthritis and in my cases of rickets the joint cartilage is entirely passive and there is no enchondral ossification; simple substitution of cartilage by fibrous bone marrow takes place. With hypertrophic arthritis the joint cartilage proliferates and is replaced by bony tissue under enchondral ossification. There is rejuvenescence of articular cartilage in cases of hypertrophic arthritis, while in cases of atrophic arthritis and late rickets the cartilage is passive.

In some regions in which there was dissecting absorption of joint cartilage, two zones of preparatory calcification could be seen, defective it is true, corresponding to the associated hypocalcemia, but present nevertheless, and parallel to each other; one (the older) bordering directly on the subchondral marrow spaces and the other forming the upper border of the dissecting marrow space. One might think that one dealt in these cases with the manifestation of a remission in the rachitic process, which often leads to the parallel arrangement of cartilage calcification in the proliferated and widened epiphysial plates. Such an assumption, however, can easily be ruled out, because the strip of cartilage interposed between the two zones of calcification was free from cellular proliferation, that is, it did not represent a zone of cartilage proliferation, and the two zones of calcification belonged to two

different processes of enchondral ossification, which were entirely independent from each other (figs. 8 and 9). However, the fact that there was a zone of preparatory calcification makes one think that most of the resorptive changes at the lower surface of the joint cartilage, atypical as they were, nevertheless were somehow related to the physiologic enchondral ossification of the joint cartilage. They had become modified, often to such a degree that from a histologic standpoint they did not even suggest enchondral ossification.

There is still the question why there should be dissecting absorption of joint cartilage if there is no enchondral ossification. As a reason may be advanced the assumption that the absorbing marrow spaces could

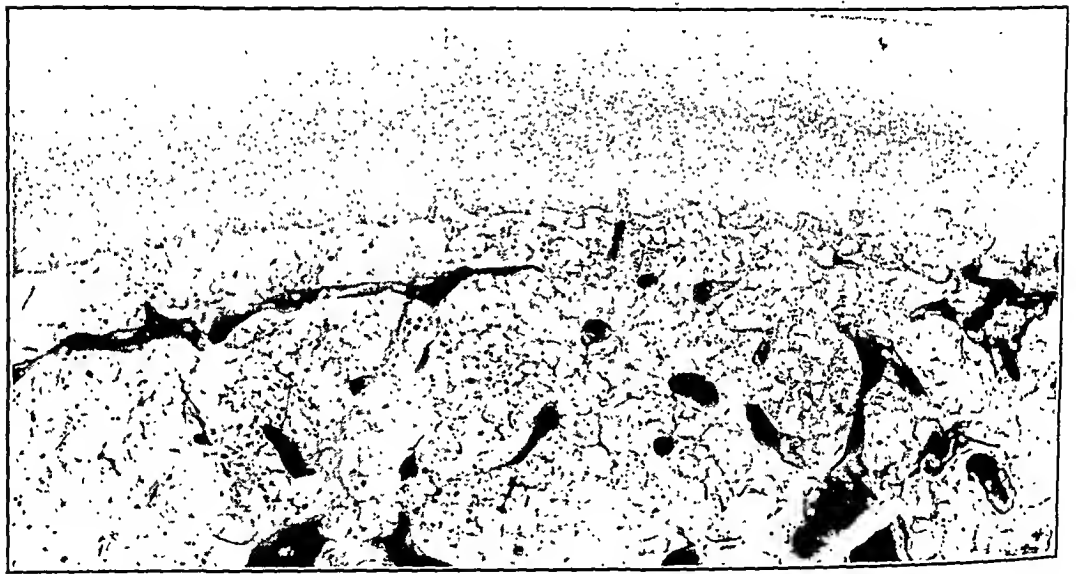


Fig. 8 (case 2).—Condyle of the femur, enlarged about 18 times. This photomicrograph is a good demonstration of loss of joint cartilage by smooth absorption from below. A series of bony trabeculae running parallel to the lower surface of the joint cartilage still indicates the level of the former subchondral hard substances. The cartilage yields by smooth absorption without formation of fibrous bone marrow. There is a marked degree of marantic atrophy of fatty bone marrow.

expand much more easily in the middle layer of the joint cartilage, where the intercellular ground substance is edematous and much softer and the cells showed more proliferation than in the deepest layer.

FIBROUS TISSUE PANNUS

Owing to the complete inactivity of the joints, the discovery of a fibrous tissue pannus extending from the joint margin over the free surface of the joint was nothing unusual, and some of the joints revealed

FREUND—JOINT CARTILAGE IN LATE RICKETS

even partial obliteration of the joint space. A synovial pannus formed at the site of reflexion and firmly united the joint cartilages of both antagonists without visible alteration of the cartilage structure, producing fibrous ankylosis due to long-lasting inactivity.

DEFORMATION OF JOINT SURFACE

It is surprising that the extreme atrophy of the joint ends had not led in more frequent instances to deformation of the joint cartilage. There is no doubt that the undermined joint cartilage lacked solidity and could have been impressed easily by a relatively mild trauma. Only the

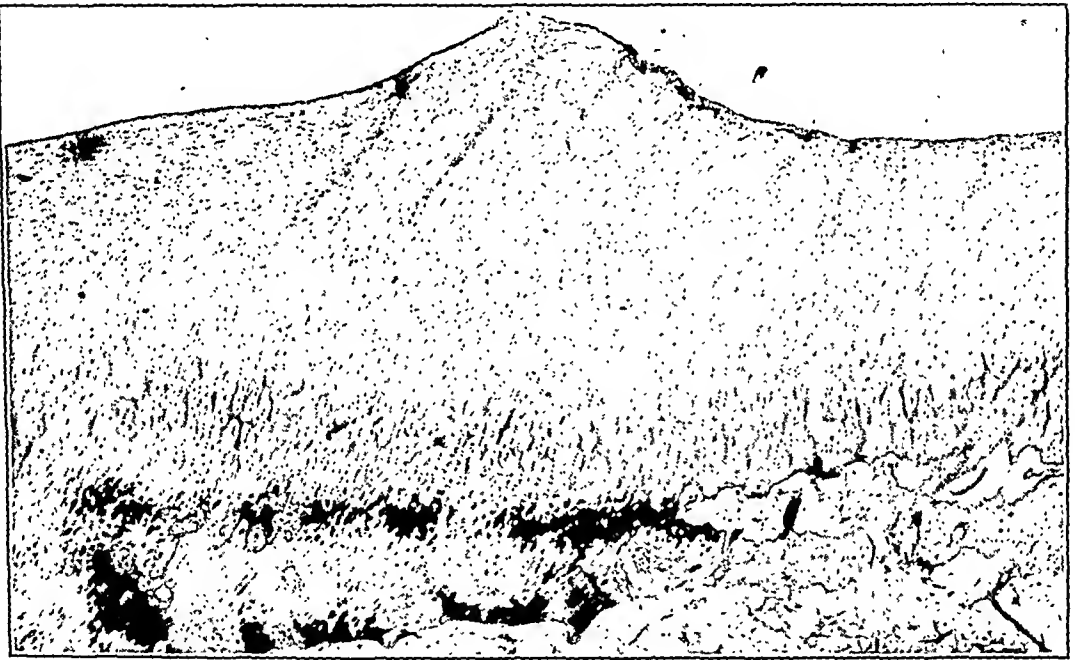


Fig. 9 (case 2).—Condyle of the femur, enlarged about 27 times. Note the dissecting absorption of the joint cartilage and also the enlargement of marrow spaces within the lower half of the joint cartilage. The expansion of the marrow spaces follows primitive and irregular calcification of joint cartilage at a higher level than the true zone of cartilage calcification could be expected. The dark streaks through the cartilage are artificial and are caused by the unevenness of the section. There is absorption of the joint cartilage from above by a fibrous tissue pannus.

lateral condyle of the femur in case 3 showed unevenness of the joint surface and an extensive callus formation of primitive fibrous osteoid in the subchondral zone. This suggested that a fracture had occurred through the extremely porotic bone, although there were no additional histologic signs of fractured bony trabeculae. This fracture had also

drawn the joint cartilage into participation. The cartilage at the joint margin showed irregular fold formation, which was partly active, owing to cartilage proliferation and elevation of the joint surface, and partly passive, owing to the extreme osteoporosis of the epiphysis and the mechanical displacement of the joint cartilage toward the bone marrow. The folded joint cartilage lacked normal structure. It had lost hyaline ground substance to a considerable degree, while the cartilage cells showed more active proliferation than was observed in any other part of the various joints. The picture changed thus by absorption of the hyaline cement substance from hyaline cartilage to fibrous cartilage and even to simple fibrous tissue. The proliferating cartilage cells reduced the intercellular septums of ground substance more and more to a rather regular network in the meshes of which lay the proliferated cartilage cells. The folded cartilage, despite its proliferation, was much thinned by smooth absorption from the bone marrow. Not fastened to the subchondral hard substances, the proliferating joint cartilage had a chance to expand to the sides as well as in height. (As long as joint cartilage is fixed by its calcified layer to the underlying bone, it can by proliferation increase only in thickness.) The increase in thickness was less noticeable because of the fact that there was constant and fairly active absorption from below. The expansion to the sides, however, led to the pleat formation as an adaptation to the disproportion between the size of the bony epiphysis and the enlarged cartilaginous cap. It is certainly remarkable that fold formation, such as I have seen in a number of different cases and even in the atrophic joints of senile persons, is such a rare observation in cases of late rickets. The almost complete inactivity of the joints, which keeps away the traumatic factor necessary for the passive form of fold formation on one side, and the lack of cartilage proliferation, which prevents the active form on the other, explain the rarity.

The surface of the folded cartilage was covered by a rather dense fibrous tissue pannus with synovial endothelium. It was especially thick over the valleys of the folds, in which the fibrous tissue was looser and contained a few capillary vessels. This somewhat smoothed the unevenness of the surface. The cells of the superficial cartilage layers under the pannus showed widening of the cell cavities and activity of the cartilage cells which changed to fibrocytes—Weichselbaum's lacunae. By confluence of several lacunae the joint cartilage changed to fibrous tissue. This was the third factor which led to thinning of joint cartilage.

INCOMPLETE ABSORPTION OF CARTILAGE

Another change of joint cartilage (fig. 10) should be mentioned. Almost the entire lower half of the thickness of the articular cartilage had lost the hyaline character; most of the cement substance had dis-

appeared, and the collagenous fiber bundles of the cartilage were clearly visible in almost straight perpendicular formations. Most of the cartilage cells freed from the surrounding cement substance had made a retrogressive change and appeared as fibroblasts, many only as shadows

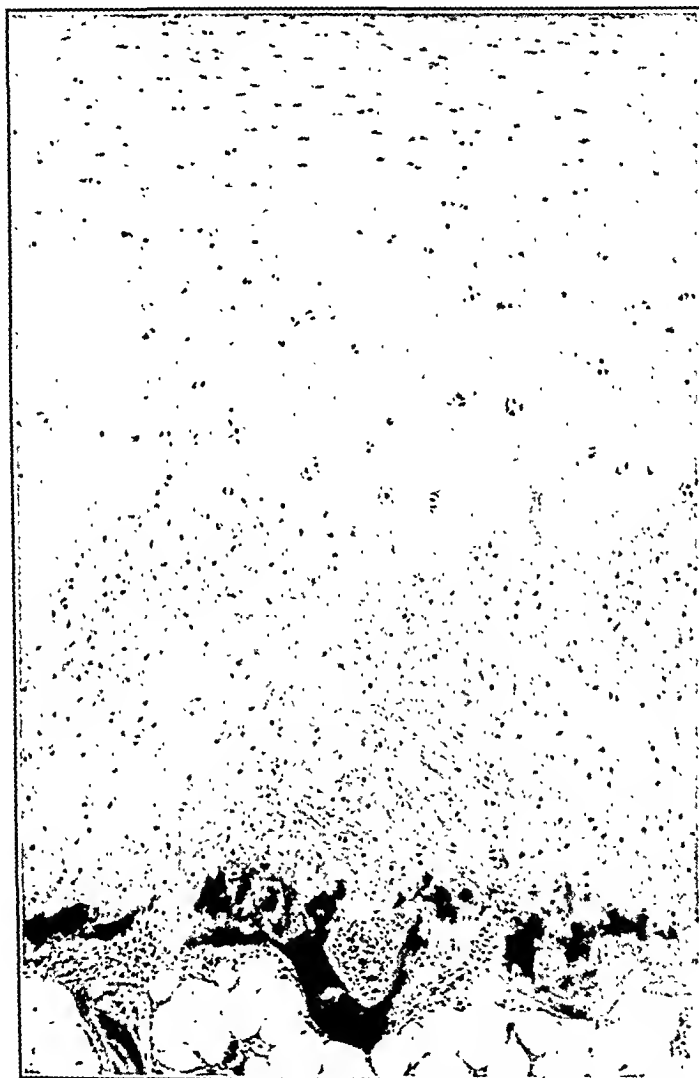


Fig. 10 (case 1).—Head of the humerus, enlarged about 75 times. Note the fibrous degeneration of the lower half of the joint cartilage. Note also the necrosis of a great number of cartilage cells within the fibrous area and the even more general necrosis in the neighboring hyaline cartilage.

but some having their spherical shapes intact. The picture was that of dense fibrous cartilage similar to a semilunar cartilage. This fibrous zone gradually blended into the more superficial layers, in the hyaline ground substance of which the collagenous fibers were firmly anchored.

A number of the freed cartilage cells proliferated and formed cellular areas. The superficial layers showed an unusually large number of necrotic cells close to the borderline between fibrous and hyaline cartilages.

It is a question to what this most unusual change of hyaline joint cartilage can be attributed. It certainly was not one of the more common damages of joint cartilage, caused by ultraphysiologic pressure or by disuse. There was little to suggest a more severe trauma which might have caused a sudden and strong compression of the cartilage, although I have seen a similar picture in the fractured head of a femur,⁷ and in that instance there was no doubt that a sudden compression, probably taking place at the moment when the fracture occurred, had altered the structure of the traumatized cartilage so severely that it appeared fibrous. The histologic picture could, again, suggest a nutritional deficiency of the joint cartilage, which resulted in the decomposition of the hyaline cement substance. The aforementioned softening of portions of the pressure layer and edema of the ground substance may be preceding stages of such decomposition.

Summarizing, I may say that joint cartilage in cases of late rickets presents a number of interesting changes which partly are associated symptoms of the general atrophy of the skeleton; in part, however, they seem to be due to an intrinsic nutritional disorder. How far the specific rachitic damage of joint cartilage goes is, of course, hard to determine by simple histologic examination. Edema and decomposition of hyaline ground substance are apparently direct consequences of avitaminosis, as is also the lack of cartilage calcification and enchondral ossification. The extreme atrophy of the joint cartilage may in part be due directly to the rachitic process and to the general hypoplasia connected with it; in part, however, it represents a nonspecific change caused by inactivity of the joints.

One has become accustomed since publication of the work of Mikulicz to attribute static deformities of the lower extremities to a late rachitic process occurring during adolescence. Irregularities in the epiphyseal plates, especially of the lower end of the femur and the upper end of the tibia, with inequality of growth caused by the disturbance of enchondral ossification, may explain a number of occurrences of genu valgum or genu varum. However, one should also consider the faulty enchondral ossification of the joint cartilage as a possible source of deformity. There is no doubt that the bony epiphyses grow by enchondral ossification of joint cartilage, and even a small irregularity or imbalance in this process must necessarily lead to disalignment of the extremity. Owing to the relative slowness of ossification of joint carti-

7. Freund, E.: *Virchows Arch. f. path. Anat.* **277**:326, 1930.

lage it is hard to evaluate such changes correctly, but the smallness of the epiphyses after the occurrence of rickets in childhood suggests that cessation of enchondral ossification of the joint cartilage occurred while the diaphysis continued to grow. I pointed out in a recent article the great importance of enchondral ossification of the joint cartilage for the acquisition of the final normal shape of the joint ends. In the case of a spastic idiot with joint contractures considerable deformities of the epiphyses had developed owing to slow or inactive enchondral ossification of those portions of the joint which were out of contact with the antagonist. The joint cartilage in these areas was atrophic and underwent absorption. Large defects in the end of the joint were thus able to develop. Similar deformities may result from inactivity and slowness of enchondral ossification in cases of severe late rickets. The imbalance of enchondral ossification of the joint cartilage explains many other deformities, especially congenital, for instance, clubfoot and dislocation of the hip. There is no doubt that enchondral ossification of joint cartilage is of far greater importance for the future shape of the extremity than it has been considered.

TREATMENT OF POSTOPERATIVE PARATHYROID INSUFFICIENCY WITH DISSOLVED CALCIUM LACTATE

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Parathyroid insufficiency is fortunately a comparatively rare complication following surgical treatment of the thyroid gland. Boothby¹ stated that 88 patients with this condition were treated at the Mayo Clinic between 1924 and 1929. This included patients operated on elsewhere as well as persons from the group on whom 13,300 thyroidectomies were performed at the clinic during this period. Because of the possibility of its occurrence, however, every surgeon should be familiar with the treatment of the condition.

MacCallum and Voegtlin in 1909 advanced the hypothesis that parathyroid tetany is due to a withdrawal of soluble and physiologically available calcium salts from the blood and especially from the nervous system. More recently McLean, Barnes and Hastings² have shown that the parathyroid glands control the concentration of the calcium ions in the blood plasma. Various methods of treatment have been reported, the most common being the use of various calcium salts, cod liver oil (or some form of vitamin D) and parathyroid extract. The basic principle of all methods of treatment is to supply the deficiency of usable calcium in the blood plasma.

Calcium lactate is the calcium salt most frequently used in the treatment of postoperative parathyroid insufficiency. Excellent results have been reported by Boothby as following the administration of cod liver oil and of calcium lactate dissolved in water. He stated that it is rarely necessary to give parathyroid extract or intravenous injections of calcium.

From the Starling-Loving University Hospital, Ohio State University.

1. (a) Boothby, W. M.: A Case of Parathyroid Insufficiency, *Proc. Staff Meet., Mayo Clin.* **7**:361-363, 1932; (b) Treatment of Postoperative Parathyroid Deficiency, *ibid.* **10**:87-91, 1935. (c) Boothby, W. M., and Davis, A. C.: Treatment of Postoperative Parathyroid Insufficiency, *Arch. Int. Med.* **58**:160-184, (July) 1936. (d) Boothby, W. M.; Haines, S. F., and Pemberton, J. de J.: Postoperative Parathyroid Insufficiency, *Am. J. M. Sc.* **181**:81-96, 1931.

2. McLean, F. C.; Barnes, B. O., and Hastings, A. B.: Influence of Thyro-Para-Thyroidectomy and a Parathyroid Hormone upon the State of Calcium in Serum of the Cat, *Proc. Soc. Exper. Biol. & Med.* **32**:253-255, 1934; The Relation of the Parathyroid Hormone to the State of Calcium in the Blood, *Am. J. Physiol.* **113**:141-149, 1935.

A review of the available experimental and clinical observations reveals a vast difference of opinion as to the effect of the oral administration of calcium lactate on the calcium content of the serum. Halverson, Mohler and Bergeim³ studied the calcium content of human blood serum and the effect of the administration of calcium lactate in normal persons and in patients with pathologic conditions. The method of oral administration of calcium lactate is not stated. An elevation of only a milligram or less was observed even after administration of 5 Gm. daily. Voegtlin⁴ stated that the oral administration of calcium is of doubtful value. Clark⁵ found calcium lactate to be the only calcium salt acceptable by animals. The feeding of a diet containing 2 per cent of calcium lactate had no effect on the calcium content of the blood. Denis and Minot⁶ gave 6 Gm. of calcium daily for a period of six to ten days to normal persons and produced no elevation of the calcium content of the plasma. Only daily determinations were made. In some cases they were able to raise the calcium content of the plasma in cats and rabbits when the initial concentration was low.

Luckhardt and Goldberg⁷ were the first to report an elevation in the plasma calcium after oral administration of calcium lactate. They were able to preserve the lives of parathyroidectomized dogs by the administration by stomach tube of 10 Gm. of calcium lactate twice daily, dissolved or partially suspended in water, and 20 Gm. daily, ground in meat. They stated definitely that their article was written because of previous reports that oral administration of calcium salts was without benefit and that it seemed absurd to give enormous quantities of calcium daily by venoclysis. The importance of dissolving the calcium lactate was apparently not realized. Jansen⁸ reported no elevation in the

3. Halverson, J. O.; Mohler, H. K., and Bergeim, O.: The Calcium Content of the Blood Serum in Certain Pathological Conditions, *J. Biol. Chem.* **32**:171-179, 1917.

4. Voegtlin, C.: The Physiological and Pathological Importance of the Parathyroid Gland from the Experimental Aspect, *Surg., Gynec. & Obst.* **25**:244-249, 1917.

5. Clark, G. W.: Effect of Hypodermic and Oral Administration of Calcium Salts on the Calcium Content of Rabbit Blood, *J. Biol. Chem.* **43**:89-95, 1920.

6. Denis, W., and Minot, A. S.: Effects of Feeding with Calcium Salts on the Calcium Content of the Blood, *J. Biol. Chem.* **41**:357-361, 1920.

7. (a) Luckhardt, A. B., and Goldberg, B.: Preservation of the Life of Parathyroidectomized Dogs, by Means of Oral Administration of Calcium Lactate, *J. A. M. A.* **80**:79-80 (Jan. 13) 1923. (b) Luckhardt, A. B., and Blumerstock, J.: Additional Observations on Completely Thyroparathyroidectomized Dogs, *Am. J. Physiol.* **63**:409-410, 1922-1923.

8. Jansen, W. H.: Kalkstoffwechsel, Blutkalkgehalt und Kalkwirkung, *Klin. Wchnschr.* **3**:715-719, 1924.

calcium content of the blood after the administration of calcium lactate. Hjort⁹ found that calcium lactate given by stomach tube in 5 per cent solution produced an increase of 17.4 to 48.2 per cent in the calcium content of the serum of normal dogs, the maximum elevation occurring from one to two hours after the administration. He also used thyro-parathyroidectomized dogs, and the results were the same except in the tendency to slower return to the preingestive calcium values. He explained the failure of others on the basis of too small doses and the drawing of blood after the calcium content had returned to normal. Kahn and Roe^{10a} gave calcium lactate dissolved in water in doses of 5 and 20 Gm. and produced a marked elevation of the calcium content of the serum, the average being 81 per cent. The maximum rise occurred from four to seven hours after the oral administration. The return of the blood to normal was not proportional to the dose. The serum calcium returned to normal in about fourteen hours. Bauer and Ropes¹¹ criticized severely the results of Kahn and Roe. The average elevation of serum calcium they obtained was 14 per cent with a dose of 10 Gm. Their method of administration was different in that they gave the calcium lactate followed by water and not dissolved in water. Roe and Kahn^{10b} reported that calcium lactate given to normal subjects produced a marked rise in the calcium content of the serum, a dose of 5 Gm. producing as marked a rise as did a dose of 20 Gm. and also producing an elevation sustained for a longer period. The elevation was not obtained when the calcium lactate was given in milk, a carbohydrate or a protein. They did not realize the importance of dissolving the calcium but concluded that calcium lactate should be given before meals, as food hinders the absorption. They further concluded that it is not necessary to incur the dangers of intravenous medication with calcium. Boothby stated that calcium lactate is not effective in the treatment of parathyroid insufficiency when given dry or in an emulsion and seems to be nearly valueless when given in tablet form.

An analysis of the results obtained reveals that an elevation in the calcium content of the serum has been obtained by oral administration only when the calcium lactate was dissolved in water. This fact has not been recognized by many and has not been emphasized in any investi-

9. Hjort, A. M.: The Influence of Orally Administered Calcium Salts on the Serum Calcium of Normal and Thyroparathyroprivic Dogs, *J. Biol. Chem.* **65**: 783-795, 1925.

10. (a) Kahn, B. S., and Roe, J. H.: Calcium Absorption from the Intestinal Tract in Human Subjects, *J. A. M. A.* **86**:1761-1763 (June 5) 1926. (b) Roe, J. H., and Kahn, B. S.: Absorption of Calcium from the Intestinal Tract of Human Subjects: The Influence of Foods, *ibid.* **88**:980-984 (March 26) 1927.

11. Bauer, W., and Ropes, M. W.: The Effect of Calcium Lactate Ingestion on Serum Calcium, *J. A. M. A.* **87**:1902-1904 (Dec. 4) 1926.

gative work. Because of this fact patients are of necessity subjected to intravenous injections of calcium and to indiscriminate use of parathyroid extract.

On the basis of investigative work, calcium lactate is the calcium salt of choice for oral administration. There is no change in the p_H of the blood when dissolved calcium lactate is used.¹² Calcium chloride causes depression and loss of appetite. Hjort reported the effects of calcium chloride, calcium lactate, calcium glycerophosphate, calcium carbonate and calcium bicarbonate on the calcium content of the serum when dissolved and when given orally. Calcium chloride caused an increase of 32.1 per cent in the calcium content of the serum but was not satisfactory because of gastric irritation and vomiting. Calcium glycerophosphate and calcium carbonate were less effective than calcium lactate. Calcium bicarbonate produced no elevation.

The following case illustrates the failure to relieve the tetany of parathyroid insufficiency when the calcium salts were not dissolved and the success in relieving symptoms when calcium lactate was dissolved in water.

REPORT OF CASE

B. S., a white woman aged 30, was admitted to the University Hospital with the complaint of continuous vaginal bleeding which had begun about two years prior to admission, after the delivery of her fifth child. She also complained of orthopnea, swelling of the feet and ankles and shortness of breath on mild exertion, all of about one year's duration. She had had nocturnal dyspnea for two months. There had been a progressive loss of 45 pounds (20.4 Kg.) in weight in eight months. The patient was well developed and well nourished and was not acutely ill. Slight exophthalmos was present. The thyroid gland was visibly enlarged. No palpable nodules were present. The lungs were normal. The blood pressure was 140 systolic and 60 diastolic. At the mitral, pulmonic and aortic areas there was a soft, nontransmitted systolic murmur. The abdomen was normal. There was no edema of the extremities. A pelvic examination revealed acute tenderness in both the right and the left adnexa. A diagnosis of chronic inflammation of the pelvis and toxic diffuse hyperplastic goiter was made.

A roentgenogram of the neck showed a left lateral deviation of the trachea. The basal metabolic rate was plus 38. Iodine in the form of potassium iodide was given preparatory to operation.

A subtotal thyroidectomy was done with the patient under anesthesia induced by avertin with amylene hydrate and nitrous oxide. The goiter removed weighed 90 Gm. It contained a few nodules of sizes up to 3 cm. in diameter and was largely of the diffuse hyperplastic variety, showing extensive iodine-induced colloid remission. A diagnosis of hyperplastic nodular colloid goiter was made. No parathyroid tissue was found on repeated examinations.

12. Salversen, H. A.; Hastings, A. B., and McIntosh, J. F.: The Effect of the Administration of Calcium Salts on the Inorganic Composition of the Blood, *J. Biol. Chem.* 60:327-339, 1924. Seyle, H.: On the Stimulation of New Bone Formation with Parathyroid Extract and Irradiated Ergosterol, *Endocrinology* 16:547-558, 1932.

The immediate postoperative condition was good. Seventeen hours after operation the patient noticed tingling sensations in the arms, the hands and the feet. The hands were drawn in typical tetanic position. The Chvostek and Trousseau signs were present. The calcium content of the blood serum was 8 mg. per hundred cubic centimeters and the inorganic phosphorus content 3.7 mg. Fifteen grains (1 Gm.) of calcium gluconate was given intravenously and produced relief. Six hours later symptoms again appeared and were relieved with the same treatment. On the second day after the operation the patient had mild tingling sensations of the hands, the feet and the face. Daily doses of 60 grains (4 Gm.) of calcium gluconate in tablet form were started. On the third day she again had tetanic spasms of the hands, the feet and the face. Intravenous calcium gluconate had to be used to obtain relief, and the same measure was necessary again on the fourth day, even with the oral administration of either calcium gluconate or calcium lactate in milk or in tablet form. On the fifth day the calcium content of the serum was 7 mg. and the inorganic phosphorus content 8 mg.

On the seventh day the patient again had tetanic spasms of the hands and arms. Thirty grains (2 Gm.) of calcium lactate was dissolved in water and given orally. Relief was obtained as quickly as with intravenous therapy. The following day 90 grains (6 Gm.) of dissolved calcium lactate was given; purified vitamin D in propylene glycol (drisdol) was also given. The Chvostek and Trousseau signs were still present, but the patient had no complaints. She remained in the hospital three days longer, being given 180 grains (12 Gm.) of dissolved calcium lactate and 5 drops of drisdol daily. She had no further seizures or complaints. Daily determinations of the calcium content of the serum ranged from 6.1 to 7.4 mg., and the inorganic phosphorus content increased from 3 to 5.5 mg., all determinations being made twelve hours after administration of the evening dose of calcium lactate.

She was dismissed on the eleventh day with instructions to continue the use of dissolved calcium lactate and drisdol. A week later she did a large washing without any ill effects.

On the seventeenth day she was instructed to go as long as possible without calcium or the vitamin D preparation. In twenty-four hours she had severe tetanic spasms, which were relieved with dissolved calcium lactate. In the next six days she had a few spasms but gradually became adjusted to the lack of calcium. On the forty-second day after the operation the calcium content of the serum was 6.5 mg. and the inorganic phosphorus content 4.3 mg. The basal metabolic rate was minus 13. Chvostek's sign was present in slight degree.

Because of the possibility of cataract formation and other sequelae of parathyroid insufficiency, administration of 180 grains (12 Gm.) of dissolved calcium lactate and 5 drops of drisdol was again instituted as daily treatment.

The patient had severe tetanic seizures during an infection of the upper respiratory tract, which were relieved with dissolved calcium lactate. The following day she was given 50 units of solution of parathyroid U. S. P. (in the form of parathyroid extract-Lilly). She suffered no other attacks but still complained of vaginal bleeding.

Four months after the onset of parathyroid insufficiency she was doing farm work and taking care of a bedfast patient. No apparent discomfort was noted.

Because of continued vaginal bleeding and the resulting secondary anemia she was transferred to the gynecologic service, and a hysterectomy was done by Dr. P. J. Reel. A pathologic diagnosis was made of chronic endocervicitis, chronic

salpingitis and lutean stimulation of the endometrium. The postoperative period was normal under the following regimen: parathyroid extract and dissolved calcium lactate preoperatively, parathyroid extract and Ringer's solution the day of operation and the first day after the operation and dissolved calcium lactate and drisdol by mouth beginning on the fourth day after the operation.

One year after the onset of parathyroid insufficiency the patient was still doing farm work. The secondary anemia had gradually disappeared. The calcium content remained unchanged from the previous low levels.

COMMENT

This case shows the advantages of administration of dissolved calcium lactate after failure of calcium salts given in tablet form or in milk. Previous to the administration of dissolved calcium lactate, intravenous calcium gluconate had to be given. The patient was able to leave the hospital under this type of treatment, returning from time to time for observation.

During the period in which calcium therapy was gradually withdrawn from the patient she did have a return of symptoms, but there was a gradual adjustment to the low calcium level of the blood serum. Because of the fact that experimental and clinical experience has shown that cataracts and other untoward symptoms may develop,¹³ it was considered advisable to continue the treatment. Later a successful major operation was done, and the postoperative convalescence was normal.

McLean, Barnes and Hastings concluded that the function of the parathyroid gland is to supply the calcium ions in the blood plasma and that in the presence of parathyroid insufficiency the calcium ion concentration is lowered. It is probable that calcium lactate when given in the dissolved state supplies this deficiency. The absorption of the calcium ions must be fairly rapid, as symptoms of tetany in this case were relieved in fifteen to thirty minutes.

Tetany occurred during an infection of the upper respiratory tract which is a frequent occurrence in such cases.¹⁴

The administration of vitamin D is as important as the administration of calcium. Brougher¹⁵ reported 4 cases of postoperative parathyroid insufficiency in which cod liver oil relieved all symptoms. Boothby and Davis¹⁶ in a recent review of the treatment of postoperative parathyroid insufficiency gave an excellent review of the rationale of vitamin D therapy and emphasized the difficulty in determining the

13. Cole, L.: Parathyroid Tetany and Cataract, *Lancet* 1:13-16, 1930.
Boothby.^{1a} Luckhardt and Blumerstock.^{7b}

14. McGhie, A. B.: Parathyroid Disturbances Following Thyroidectomy, with Report of a Case, *Canad. M. A. J.* 31:27-29, 1934.

15. Brougher, J. C.: Viosterol (Irradiated Ergosterol) in the Treatment of Parathyroid Tetany, *J. A. M. A.* 94:471-473 (Feb. 15) 1930.

dosage. The vitamin increases the absorption or decreases the excretion in the intestines, thus tending to produce a positive calcium balance.¹⁶

In some cases occasional injections of parathyroid extract have to be used in addition to cod liver oil and dissolved calcium lactate.¹⁶ Continued injections are not effective, as the patient acquires a tolerance to the drug. There is an initial rise in the calcium content of the serum.¹⁷ Elimination of calcium is also increased. Pugsley and Seyle¹⁸ reported the histologic picture of bone after injections of parathyroid extract. With the rise in serum calcium there are large numbers of osteoclasts, or bone-destroying cells, in the bone marrow. With continued injections these cells disappear and are replaced by osteoblasts. Formation of bone occurs, and during this process there is no elevation in the calcium content of the serum. This explains the tolerance to the parathyroid extract. With the use of calcium lactate there are retention of inorganic phosphorus and a diminished urinary excretion of phosphorus, even for normal persons.¹⁹ It has been shown that parathyroid extract causes an immediate phosphorus diuresis and a decrease in the inorganic phosphorus content of the serum of normal persons and of patients with parathyroid insufficiency.²⁰ This is probably another indication for occasional injections of the extract.

SUMMARY

A review of the literature is presented as to the effect of calcium salts, particularly calcium lactate, when given orally, on the calcium content of the blood serum of normal persons and of patients with para-

16. Harris, L. J., and Innes, J. R. M.: The Mode of Action of Vitamin D: The Influence of the Calcium-Phosphorus Intake, *Biochem. J.* **25**:368-390, 1931. Spies, J. W.; Wilson, R. H., and Stingham, J. A.: Action of Viosterol and Parathormone in Thyroparathyroidectomized Dogs, *Proc. Soc. Exper. Biol. & Med.* **28**:527-528, 1931.

17. Collip, J. B.: The Extraction of a Parathyroid Hormone Which Will Prevent or Control Parathyroid Tetany and Which Regulates the Level of Blood Calcium, *J. Biol. Chem.* **63**:395-438, 1925. Collip, J. B.; Clark, E. P., and Scott, J. W.: The Effect of Parathyroid Hormone on Normal Animals, *ibid.* **63**:439-460, 1925.

18. Pugsley, L. I., and Seyle, H.: The Histological Changes in the Bone Responsible for the Action of Parathyroid Hormone on the Calcium Metabolism of the Rat, *J. Physiol.* **79**:113-117, 1933.

19. Heyl, F. W., and Hart, M. C.: The Availability of the Calcium in Calcium Lactate in the Human, *J. Am. Pharm. A.* **17**:225-232, 1928. Robinson, C. S.; Huffman, C. F., and Mason, M. F.: The Results of the Ingestion of Certain Calcium Salts and of Lactose, *J. Biol. Chem.* **84**:257-267, 1929.

20. Ellsworth, R.: Action of Parathyroid Extract on the Renal Threshold for Phosphorus, *J. Clin. Investigation* **11**:1011-1017, 1932. Goadby, H. K., and Stacey, R. S.: On the Action of Parathormone, *Biochem. J.* **28**:2092-2094, 1934; **30**:269-272, 1936.

thyroid insufficiency. Only dissolved calcium salts produce any marked elevation in the calcium content of the serum. Calcium lactate when dissolved in water and given orally produces a marked elevation.

A case of severe postoperative parathyroid insufficiency is discussed in which calcium salts in tablet form or in milk did not relieve tetany. Calcium lactate dissolved in water gave immediate relief of symptoms. A major operation was done eight months after the onset of parathyroid insufficiency. Satisfactory medical management of the condition resulted in a normal postoperative convalescence.

The staff of the Division of Gynecology, Department of Surgery, and the staff of the Department of Surgical Research permitted me to follow the case reported in this paper. The staff of the Department of Surgical Research gave technical assistance in determining the values for phosphorus and calcium.

MECHANICAL INTESTINAL OBSTRUCTION COMPLICATING PELVIC INFLAMMATORY DISEASE

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Intestinal obstruction caused by gynecologic disease is infrequent. Reports of obstruction due to strangulation of the intestine by a cyst pedicle, to hernia into the broad ligament or to endometriosis have been found. There have been few reports of intestinal obstruction associated with pelvic inflammatory disease; the following discussion will be confined solely to this particular complication.

McIver stated that tubal inflammation may result in intestinal obstruction.¹ However, in review of 21 cases of obstruction caused by bands (without previous laparotomy), he cited no case in which pelvic inflammatory disease was the cause.² Treves³ wrote, "I have knowledge of several instances in which 'pelvic inflammation,' 'meritis,' or 'pelvic cellulitis,' appears without doubt to have provided the band." Norris,⁴ in his treatise "Gonorrhea in Women," did not even mention intestinal obstruction as a complication. Kaufman⁵ reported a single case of ileus complicating salpingitis. Vanderzypen⁶ and Martens⁷ have each reported 2 cases, and Thaler⁸ 3 similar cases. Holtz,⁹ in 1,262 cases

From the gynecologic service of the Harlem Hospital, H. C. Falk, M.D., Director.

1. McIver, M. A.: *Acute Intestinal Obstruction*, New York, Paul B. Hoeber, Inc., 1934.

2. McIver, M. A.: *Acute Intestinal Obstruction*, *Arch. Surg.* **25**: 1106 (Dec.) 1932.

3. Treves, F.: *Intestinal Obstruction*, Baltimore, William Wood & Company, 1889.

4. Norris, C. C.: *Gonorrhea in Women*, Philadelphia, W. B. Saunders Company, 1913.

5. Kaufman, M. R.: *Occlusion intestinale aiguë*, *Gynécologie* **29**: 603, 1930.

6. Vanderzypen: *L'occlusion intestinale d'origine gynécologique*, *Bruxelles-méd.* **16**: 800, 1936.

7. Martens, M.: *Ueber mechanischen Ileus bei acut-entzündlichen abdominal Erkrankungen*, *Deutsche Ztschr. f. Chir.* **86**: 508, 1907.

8. Thaler, H.: *Die entzündlichen Adnex-und Bindegewebserkrankungen*, *Arch. f. Gynäk.* **93**: 413, 1911.

9. Holtz, F.: *Klinische Studien über die nicht tuberkulöse Salpingo-oophoritis*, *Acta obst. et gynec. Scandinav. (supp.)* **10**: 1, 1930.

of tuberculous salpingo-oophoritis, found only 1 case of intestinal obstruction. Flesch-Thebesius¹⁰ in 162 cases of mechanical ileus due to adhesions found the condition to be of gynecologic origin in 15; in 8 it was caused by parametritis, and in 7, by salpingitis. Turunen¹¹ reported 12 occurrences of mechanical ileus in 3,025 cases of adnexitis caused by abortion, by infection during delivery or by gonorrhea. Of these, 10 occurrences were due to stringlike adhesions, and 2 were caused by agglutination of loops of intestine. Usually the complication occurred after long-standing inflammation; in only 2 cases had the symptoms of pelvic inflammatory disease been present for less than one month. The mortality in this series was 47.7 per cent.

Mechanical intestinal obstruction complicating pelvic inflammatory disease is uncommon, but it does occur. In an active gynecologic service to which approximately 60 per cent of all admissions are for pelvic infection, either postabortal or gonorrheal, attention was called to this complication by its occurrence in 2 cases within one month. An additional case was found in the hospital records of ten years ago.

REPORT OF CASES

CASE 1.—A. C., a Negress aged 42, married, was first admitted to the hospital on Oct. 14, 1927. She was a bipara and had had five pregnancies. She complained of pain in the abdomen, which had begun suddenly four days previously and had become progressively worse. Pain in the chest had been present for the past day. The menses began at the age of 13; they were regular, and the periods lasted three days. The date of the last period was uncertain, although the patient said she was not pregnant. She had had an abortion fourteen years before. The temperature was 105 F., the pulse rate 160 and the respiratory rate 34. The patient appeared prostrated and showed indefinite signs of consolidation in the chest (which rapidly cleared). The abdomen was distended and tympanitic. Tenderness, rebound and rigidity were present, particularly in the left hypogastrium. Vaginal examination showed the cervix to be cone shaped and flattened; the external os was closed. The fundus of the uterus was small and anterior. A large mass was felt in both cul-de-sacs, extending upward to an indefinite point near the umbilicus. The white blood cell count was 24,000, with 96 per cent of polymorphonuclears. A diagnosis of postabortal pelvic cellulitis was made.

The temperature ranged up to 103 F. for three days, after which softening occurred. Colpotomy was then performed, with evacuation of a large amount of pus. Despite the colpotomy, the temperature did not return to normal until the twenty-eighth day after the operation. During this period, digital dilation of the colpotomy opening, injections of milk given intramuscularly and vaginal diathermy were used, with gradual subsidence of the parametrial masses. On the forty-fourth day after the operation the patient appeared well; the temperature was

10. Flesch-Thebesius, M.: Ueber Ileus durch Verwachsungen und Stränge, *Deutsche Ztschr. f. Chir.* 157: 60, 1920.

11. Turunen, A. O.: Ueber den Darmverschluss als Komplikation von Krankheiten und Operationen der inneren Geburtsteile, *Acta obst. et gynec. Scandinav.* 12: 421, 1932.

normal, no symptoms were present and there were no physical signs except for slight induration in the fornices. On this day there was a sudden onset of colicky abdominal pain, vomiting and generalized rigidity, with tenderness at McBurney's point. The white blood cell count was 21,000, with 90 per cent of polymorphonuclears. Enemas were not effectual. On the following day, the patient appeared worse; pain and vomiting continued, and she was operated on. The preoperative diagnosis was mechanical intestinal obstruction.

At operation, 300 cc. of straw-colored fluid was found in the abdomen. The small intestine was distended and injected. The loops were followed until a loop of the lower part of the ileum was found to be bound down to the broad ligament and to be kinked at this point. Below the kink the intestines were collapsed. The pelvic peritoneum and the pelvic organs appeared to be normal. The adherent kinked loop of intestine was freed from the broad ligament, and the distal portion of the intestine immediately ballooned out with gas. The patient made an uneventful recovery and was discharged on the twenty-sixth day after the operation (Dec. 23, 1927).

CASE 2.—M. B., a Negress aged 16, single, was first admitted to the hospital on Nov. 25, 1936, complaining of pain in the abdomen for the past five weeks, accompanied by vaginal discharge, burning on urination, frequent voiding and nocturia. The pain was most pronounced in the right lower quadrant of the abdomen. It began immediately after a menstrual period five weeks before her admission. She vomited several times the night before admission. The menses began at the age of 11; they were regular; the periods lasted four days and were unaccompanied by pain. The last normal period was one week before admission. The temperature was 98.6 F., the pulse rate 80 and the respiratory rate 24. The patient appeared moderately ill. The abdomen was soft, and tenderness was present in both lower quadrants. There was no distention, no rigidity and no rebound. Vaginal examination showed the uterus to be anteverted; a tender sausage-shaped mass was present in each fornix. The white blood cell count at this time was 21,000, with 80 per cent of polymorphonuclears. The impression was that a bilateral pyosalpinx existed with moderate pelvic peritonitis. An enema given in the evening of the same day was effectual.

For four days the temperature was below 100 F. On the fifth day, the temperature rose to 100.4 F. and the patient suddenly appeared acutely ill. The abdomen was diffusely tender and was distended. It was thought at this time that peritonitis due to a leaking pyosalpinx was present. An enema returned fluid stained with fecal material, but no gas. The distention, tenderness, vomiting and rigidity increased in severity. A Harris drip instituted at this time was ineffectual. The temperature rose to 101.6 F. just before death, and the patient died eight days after admission (Dec. 3, 1936), four days after the occurrence of what was interpreted as being a "leaking tube" with peritonitis.

Autopsy revealed nothing abnormal except in the abdomen. A loop of ileum was pulled down, bound and kinked by a fibrous adhesion which extended from the serosal surface of a loop of intestine to the posterior wall of the pelvis, in the region of the sacrum—about 6 inches (15 cm.) of the ileum was bound down firmly and completely obstructed by this adhesion. The small intestine proximal to the adhesion was dilated; the intestine below the adhesion was collapsed. The adhesion itself was grayish and vascular and measured 2 inches (5 cm.) in length and 3 inches (7.5 cm.) in thickness. Numerous rather firm adhesions were present in the pelvis, which bound the uterus and tube to the bladder and rectum. There were also fine adhesions between the liver and the

diaphragm; these were of the "violin string" type. There was a right pyosalpinx, and the ovaries appeared normal. The diagnosis was fibrous adhesion extending from the serosa of the ileum to the anterior wall of the sacrum; strangulation of the ileum; right pyosalpinx; pelvic adhesions; perihepatitis; dehydration. The cause of death was acute mechanical intestinal obstruction.

CASE 3.—J. B., a nulliparous Negress aged 19, single, was first admitted to the hospital on Nov. 16, 1936. She complained of pain in the lower part of the abdomen and in the back for two weeks, associated with vaginal discharge for ten days. These symptoms became progressively more severe and were associated with fever. No vomiting occurred. There was a history of an abortion two years previously. The menses began at the age of 13; they were regular, and the periods lasted four days. The last normal period was seventeen days prior to admission. On the day of admission to the hospital the menses reappeared; this period was nine days earlier than usual. The temperature was 101 F., the pulse rate 108 and the respiratory rate 24. The patient appeared acutely ill and complained of severe pain in the lower part of the abdomen. The abdomen was rigid. Tenderness and rebound were present in both lower quadrants. Vaginal examination showed the cervix to be short, conical and closed; a brownish, bloody discharge was present. Pain was elicited on movement of the cervix. The uterus was small and retroverted, and there was an extremely tender sausage-shaped mass in each fornix, closely applied to the uterus. The white blood cell count was 9,960, with 84 per cent of polymorphonuclears. The sedimentation rate was 18 mm. in twenty minutes. The diagnosis was bilateral pyosalpinx, pelvic peritonitis and retroversion of the uterus.

With palliative therapy, the patient's temperature ranged between 100 and 102.4 F. for one week. The temperature thereafter was constantly below 100 F., the abdominal signs subsided and the patient was apparently recovering. She was allowed to be out of bed on the sixteenth day; that evening she had a sudden recurrence of symptoms, with abdominal pain and vomiting. There was moderate tenderness and rigidity in the lower part of the abdomen; an enema was effectual. On the following day (the seventeenth day of hospitalization), she continued to vomit and to complain of cramplike pain. The temperature was 100 F.; the lower part of the abdomen was distended, tympanitic, tender and rigid. Because of the sudden onset of cramplike pain, mechanical obstruction was suspected, rather than paralytic ileus caused by recurrence of the peritonitis. A Harris drip was given, and liquid petrolatum was introduced into the duodenum by means of a Levine tube. No oil, gas or feces was recovered in the Harris drip in twelve hours. A flat roentgenogram of the abdomen taken on the same day showed distended loops of small bowel (with fluid levels) and no evidence of gas in the large intestine. The diagnosis of mechanical obstruction of the small bowel was thus confirmed, and a laparotomy was performed that evening. At operation, 20 cc. of free straw-colored, odorless fluid was found in the peritoneum. There were many fresh fibrinous adhesions between loops of ileum, resembling violin strings. The small intestine was distended and somewhat congested. The distended loops were followed toward the cecum until a firm adhesion band was found 4 inches (10 cm.) proximal to the ileocecal junction, causing complete occlusion of a loop of ileum. This band ran from the serosa of the ileum to the pelvis; distal to the band the ileum was completely collapsed. As soon as the adhesion was severed the collapsed intestine ballooned out. The pelvic organs were rapidly palpated, and the adnexa were found to be subacutely inflamed. The patient made an uneventful recovery and was discharged on December 26, the eighteenth day after the operation. An examination of the pelvis at this time revealed small, slightly tender masses in each fornix.

ETIOLOGY AND PATHOGENESIS

The fundamental methods by which bands of adhesions produce strangulation are well known. McIver¹ stated:

Bands form bridges or arches under which intestinal loops become engaged or strangulated, or long cords are formed into nooses or knots which capture a loop. Of these two types, strangulation under bands is more frequent. All that is essential for strangulation is a firm band attached at two points to form an arch and a firm surface to make the floor of the arch.

Bands are congenital or inflammatory in origin. Primary inflammatory bands (without previous laparotomy) are rarely seen today, since they are the result of peritonitis following appendicitis or ruptured gastric ulcer; in such cases the condition is usually diagnosed early, and the patient is operated on before firm adhesions form. However, pelvic peritonitis, for which the usual treatment is conservative and operation is deferred, presents favorable opportunity for the formation of inflammatory bands. Treves stated:

Where the isolated adhesion is due to pelvic peritonitis, it may be found to be attached by one end to some pelvic viscus and by the other to a neighboring part. Thus bands are found passing from the uterus, ovary or bladder to the parietal peritoneum of the pelvis or abdomen; or starting from the same source, they may attach themselves to the cecum or sigmoid flexure, or with much greater frequency to some part of the lower ileum or its mesentery. In several instances, the constricting band has merely passed from one point on the pelvic wall to another.

The occurrence of adhesive bands after acute salpingitis has not been generally recognized. Another fact frequently overlooked is that the accompanying primary peritonitis may be widespread. Curtis¹² has described violin string adhesions about the liver in cases of chronic salpingitis; he stated the opinion that these adhesions are the end result of acute inflammation. Fitz-Hugh¹³ has recovered the gonococcus from the drainage tract after a laparotomy for acute perihepatitis. Therefore, since it is recognized that salpingitis may cause pelvic and generalized peritonitis with the secondary formation of bands, it can readily be seen how mechanical intestinal obstruction may occur. Falk¹⁴ has shown that general peritonitis may be caused by postabortal infection by direct extension through the tubes. In such a case the condition is usually of streptococcic origin and results in death within two to

12. Curtis, A. H.: (a) Adhesions of the Anterior Surface of the Liver, *J. A. M. A.* 99: 2010 (Dec. 10) 1932; (b) *Obstetrics and Gynecology*, Philadelphia, W. B. Saunders Company, 1933, vol. 2, chap. 42, p. 448.

13. Fitz-Hugh, T., Jr.: Acute Gonococcic Peri-Hepatitis: A New Syndrome of Right Upper Quadrant Abdominal Pain in Young Women, *Rev. Gastroenterol.* 3: 125, 1936.

14. Falk, H. C.: Abortion, *Am. J. Surg.* 35: 187, 1937.

three weeks. This does not allow sufficient time for adhesions to form. However, in cases in which postabortal infection causes pelvic cellulitis, intra-abdominal adhesions may occur, although the condition is primarily extraperitoneal. The mechanism by which this is produced is believed to be as follows:

1. Subperitoneal cellulitis may cause edema of the peritoneum, with exudation on the peritoneal surface, resulting in a roughened peritoneum and in local peritonitis.¹⁵

2. Pelvic cellulitis may produce peritoneal blebs; pinpoint rupture of a bleb into the peritoneum may cause an adhesion to form at this site.

3. An imminent intraperitoneal perforation of an abscess of a broad ligament may be sealed off from the general peritoneal cavity by a loop of intestine becoming adherent at this point; evacuation of the abscess and healing of infection cause shrinkage of the swollen parametria, with the result that the adherent loop of intestine is drawn into the pelvis and kinked, causing obstruction.

4. The omentum may be drawn into the pelvis by one of the methods described and may act as a constricting band.

SYMPTOMS

The symptoms of this condition are like those of acute intestinal obstruction from any other cause. There is a sudden onset of vomiting, of distention and of cramplike pain, which is unlike the unremitting pain caused by salpingitis. If the complication is not recognized early, fecal vomiting and complete obstipation result. On roentgen examination of the abdomen the typical signs of mechanical obstruction may be seen, that is, "step ladder" pattern, gas and fluid levels in the small intestine and absence of gas in the large bowel. Obstruction occurring in pelvic inflammatory disease usually appears while the inflammatory process is subsiding. In 2 of our cases the obstruction occurred late, when both patients were recovering. In the other case, although the obstruction occurred shortly after admission to the hospital, the autopsy showed that the salpingitis was of long duration.

DIFFERENTIAL DIAGNOSIS

Paralytic ileus due to peritonitis must be differentiated from mechanical obstruction. This differentiation at times may be difficult, as both conditions manifest themselves by distention, tympanites, constipation, vomiting and signs of the underlying peritoneal inflammation. Diffuse

15. Polak, J. O.: *Pelvic Inflammation in Women*, Gynecological and Obstetrical Monograph Series, New York, D. Appleton and Company, 1924.

peritonitis in gynecologic disease most commonly is caused by acute salpingitis, by "leaking" pyosalpinx, by ruptured pyosalpinx or by septic abortion. Associated with these conditions we find elevated temperature and leukocytosis as well as the local signs of acute pelvic inflammation. On the other hand, the local and general symptoms of the acute inflammation have subsided or are subsiding when the acute intestinal obstruction occurs. When there is a sudden recurrence of acute symptoms, with cramplike pain, vomiting and distention, in a patient with pelvic inflammation who is apparently recovering, mechanical obstruction must be ruled out. All patients with ileus in this service are treated with duodenal drainage (Levine tube) and a Harris drip, for both diagnostic and therapeutic purposes. It has been found that with complete mechanical obstruction there is no gas or fecal return in the drip. With paralytic ileus the drip causes sufficient peristalsis to allow some return of fecal material and gas. A further refinement in the differential diagnosis is to introduce liquid petrolatum through the tube (eight doses of 4 drachms [14.4 cc.]) at intervals of one hour. With paralytic ileus some oil will be recovered in the drip; with mechanical obstruction no oil is recovered. A flat roentgenogram of the abdomen should always be taken for evidence of mechanical obstruction.

PROGNOSIS AND TREATMENT

The prognosis is in direct relation to the time elapsing between the occurrence of obstruction and its release. If operation is performed early a recovery usually results; if the condition is not recognized or if the operation is delayed a fatality is to be expected. It is particularly important for gynecologists to differentiate early between ileus caused by peritonitis of pelvic origin and that caused by mechanical obstruction. If mechanical obstruction is not recognized or is recognized late, the period of optimum operability is lost, for the treatment of this type of obstruction is immediate laparotomy, whereas the treatment of pelvic peritonitis is essentially nonoperative in the early stages. Surgical elimination of the pelvic inflammatory mass at this time would seem injudicious.

SUMMARY AND CONCLUSIONS

Three cases of intestinal obstruction complicating pelvic inflammatory disease are reported.

The pathogenesis of this complication is discussed.

The outstanding symptom of the complication has been found to be the sudden onset of cramplike pain and distention in a patient with pelvic inflammatory disease who is apparently recovering.

It is important to diagnose this complication promptly in order to insure early surgical intervention.

TUBERCULOSIS OF THE STOMACH

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Tuberculosis of the stomach is an inflammatory granulomatous lesion of the stomach produced by the tubercle bacillus. Little was known about this condition before 1824, when a case was reported by Barkhausen.¹ Since that time, however, the subject has aroused considerable interest, and 367 additional cases have been reported. This interest has been due partially to the rarity of the condition, but it also is largely attributable to the interesting clinical problems and varied pathologic manifestations presented by the condition.

Although Barkhausen was the first to report a case of gastric tuberculosis, the condition was not definitely established as a pathologic entity until Litten's² report and classic description of the findings in a case he had observed in 1876. Four years after the discovery of the tubercle bacillus by Koch in 1882, Coats³ reported a case in which he was able to demonstrate the tubercle bacillus in the depths of the lesion. He thus became the first to report a proved instance of gastric tuberculosis. Since that time numerous reports of single cases and several extensive reviews of series of cases collected from the literature have been published. Notable among these have been the review by Arloing⁴ in 1902, that by Ricard and Chevrier⁵ in 1905, that by Broders⁶ in 1917 and that by Good⁷ in 1929.

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1. Barkhausen, cited by Broders.⁶

2. Litten, M.: *Ulcer ventriculi tuberculosum*, Virchows Arch. f. path. Anat. **67**:615-617 (Aug.) 1876.

3. Coats, J.: *On a Case of Tuberculosis of the Stomach, and One of Acute Miliary Tuberculosis Depending on Tuberculosis of a Pulmonary Vein, with Remarks on the Pathology of These Conditions*, Glasgow M. J. **26**:53-61, 1886.

4. Arloing, F., cited by Broders.⁶

5. Ricard and Chevrier: *De la tuberculose et des sténoses tuberculeuses du pylore*, Rev. de chir., Paris **31**:557-586 (May) 1905.

6. Broders, A. C.: *Tuberculosis of the Stomach, with a Report of a Case of Multiple Tuberculous Ulcers*, Surg., Gynec. & Obst. **25**:490-498 (Oct.) 1917.

7. Good, R. W.: *Tuberculosis of the Stomach: An Analysis of Cases Recently Reviewed*, Arch. Surg. **22**:415-437 (March) 1931.

INCIDENCE

The incidence of tuberculosis of the stomach as determined at necropsy and by the examination of surgical material has varied considerably in the reports of different investigators. The most extensive investigation of the incidence of gastric tuberculosis at necropsy was that by Glaubitt.⁸ In 1901 this investigator reported that he observed gastric tuberculosis in 47 of a series of 12,528 cases in which necropsy was performed. In 2,237 of these cases the patients had died of tuberculosis. The incidence of gastric tuberculosis, therefore, was 0.37 per cent for the entire series of cases and 2 per cent for the cases in which the patients had died of tuberculosis. Simmonds⁹ observed 18 instances (0.76 per cent) of gastric tuberculosis in 2,360 cases in which necropsy was performed. In 1929 Good collected a total of 71,871 cases in which the presence or absence of gastric tuberculosis had been recorded by various investigators. The incidence of gastric tuberculosis in this series of cases was 0.34 per cent. This probably is the most accurate figure available as to the incidence of this condition. In 15,165 of the cases in this series the patients had tuberculosis elsewhere in the body; the incidence of tuberculosis, therefore, was 1.4 per cent for the latter group of cases.

The incidence of gastric tuberculosis found at surgical exploration is particularly interesting, since it is at operation rather than at necropsy that the diagnosis should be made. Clairmont¹⁰ reported 2 instances in a series of 258 consecutive gastric operations; Demel¹¹ found 3 in 1,568 gastric explorations; and Knoflach and Pape¹² found 5 in 4,000 consecutive histologically controlled operations at the University of Vienna. Good reported 3 instances in 7,416 consecutive gastric operations at the Mayo Clinic. The average incidence of gastric tuberculosis found on gastric exploration in cases reported by these investigators is about 0.12 per cent. Gastric tuberculosis is certainly a rare condition, but it does deserve some diagnostic consideration, especially if there is evidence of tuberculosis elsewhere in the body.

MODES OF INFECTION

Practically all writers on the subject of tuberculosis of the stomach agree that there are four possible routes by which infection may occur: (1) through the mucosa (direct infection); (2) through the blood

8. Glaubitt, cited by Broders.⁶

9. Simmonds, M.: Ueber Tuberculose des Magens, München. med. Wchnschr. 47:317-318 (March) 1900.

10. Clairmont, P.: Bericht über 258 von Prof. v. Eiselsberg ausgeführte Magenoperationen, Arch. f. klin. Chir. 76:180-322, 1905.

11. Demel, N., cited by Knoflach and Pape.¹²

12. Knoflach, J. G., and Pape, R.: Ein Fall von polypöser, nicht ulcerierter Magentuberkulose, Wien. klin. Wchnschr. 47:1288-1290 (Oct.) 1934.

stream; (3) through the lymphatic stream, and (4) by continuity and contiguity of structure. That the stomach is highly immune to tuberculosis is beyond question. In this respect it is similar to the thyroid gland, the salivary glands, the esophagus, the pancreas, the gallbladder, the ovaries, the uterus and the heart, which are rarely the sites of tuberculous infection. Unfortunately it is not known at present what factors these organs have in common that make them resistant to tuberculosis.

There has been considerable controversy concerning the usual route of tuberculous infection of the stomach. After a review and consideration of the evidence it must be admitted that infection may occur by any of the four routes and that reasonably authentic instances of infection by each have been described. On the other hand, it must be conceded that the stomach has considerable immunity to infection by the tubercle bacillus by any route. Infection probably never occurs through the intact mucosa; it occurs through erosion, ecchymosis, gastritis, ulcer and carcinoma, which under some conditions can act as portals of entry for the infection. Retrograde lymphatic infection from the mediastinal to the perigastric lymph nodes apparently occurs not infrequently. The most common route of infection is beyond doubt the blood stream. This has been proved by the animal experiments of Arloing and Montemartini¹³ and by the bulk of clinical evidence.

The remarkable resistance of the stomach to tuberculous infection, often in the face of constant exposure to active, virulent tubercle bacilli in the sputum or in contaminated food, has been a subject of considerable interest and investigation. It has been variously attributed to the following factors: (1) the effect of the gastric juice on the tubercle bacilli; (2) the scarcity of the lymph follicles and lymphatics in the walls of the stomach; (3) the rapid emptying of the stomach; (4) the integrity of the gastric mucous membrane; and (5) resistance of muscular tissue to tuberculous infection.

Undoubtedly, no one factor is entirely responsible for the immunity of the stomach to tuberculous infection. The gastric juice has been shown by extensive experiments to be an almost negligible factor, because not only is the value for the acidity of the gastric contents usually lowered in cases of tuberculosis, but a normal gastric juice has been shown to have little or no effect on tubercle bacilli unless it is in contact with them for at least twelve hours. The sparsity of lymph follicles is probably of considerable importance, since the tubercle bacillus has a strong predilection for the lymphatic system and naturally would not be common in an organ with a meager lymphatic supply. Furthermore, the fact that the condition occurs most frequently in the pyloric region, where the lymph follicles are abundant, supports this contention. The

13. Montemartini, cited by Rodríguez Olleros and de la Viesca García.¹⁶

rapid emptying time of the stomach is doubtless a factor of major importance, since it does not allow sufficient contact of the tubercle bacillus and gastric mucosa to permit infection to occur, especially if the gastric mucosa is intact.

PATHOLOGIC CHANGES

Tuberculosis is an infectious disease caused by the tubercle bacillus. The lesion produced is variable, and the changes depend on many factors, such as the number and virulence of the organisms, their dissemination in the body and the resistance of the host. The most characteristic lesion is the tubercle (figs. 1, 2, and 3), but its structure may vary with some of the factors already mentioned. Occasionally

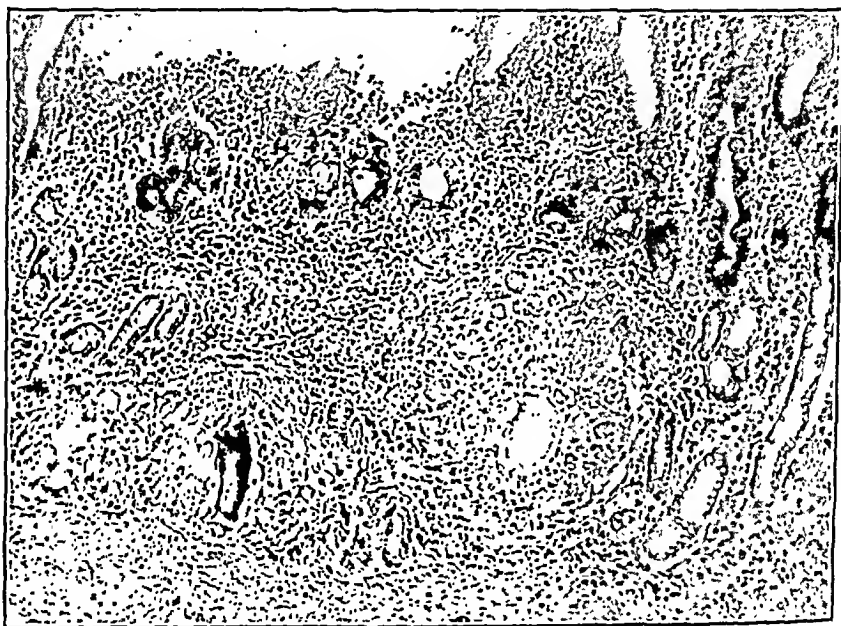


Fig. 1.—Submucous tubercles, epithelioid cells and giant cells; $\times 90$.

the tubercle bacillus may excite a diffuse, acute inflammatory reaction. The effects of infection by the tubercle bacillus may be a result of local destruction of tissue or the products of the tubercle bacillus, or both.

Although many cases of gastric tuberculosis had been reported previously, it was not until 1917, when Broders reviewed and analyzed 305 cases of gastric tuberculosis collected from the literature, that the pathologic criteria for a diagnosis were established. Broders recommended the following criteria for the diagnosis of tuberculosis of the stomach: (1) the diagnosis may be considered positive in all cases in which there is a pathologic picture of tuberculosis of the stomach plus the presence of the bacillus of tuberculosis in the depths of the lesion; (2) the diagnosis may be considered probable in all cases in which there is a

histologic picture of tuberculosis of the stomach, and (3) the diagnosis should be considered possible in all cases in which there is a good description of the gross lesions of tuberculosis of the stomach or a good

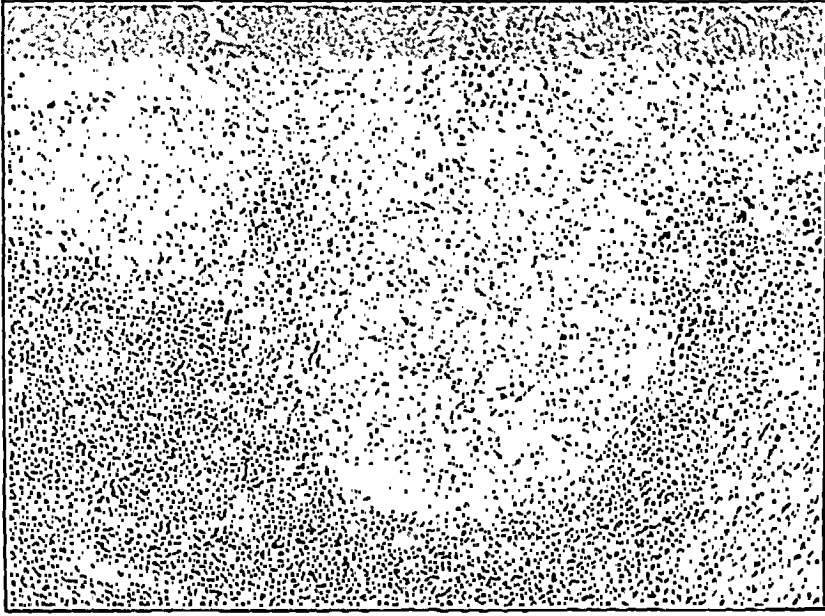


Fig. 2.—Tubercle and giant cells; $\times 100$.

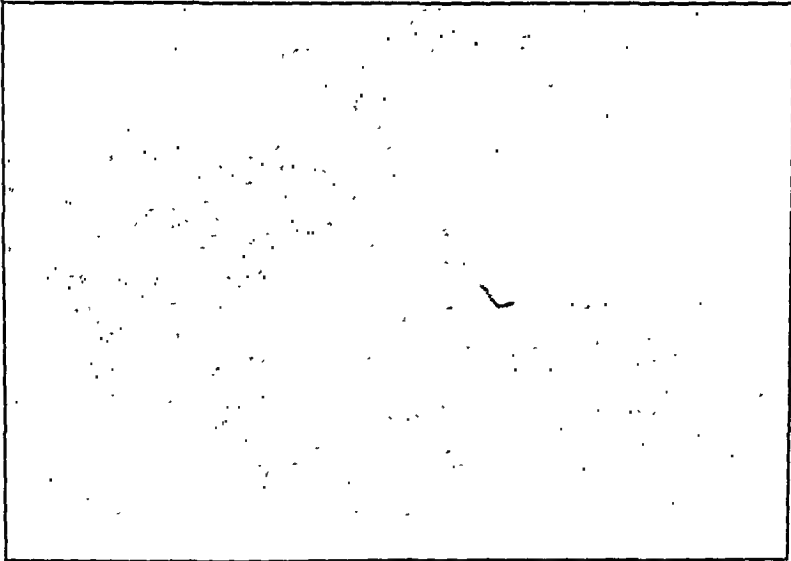


Fig. 3.—Tubercle bacillus in giant cell; $\times 1060$.

description of the gross lesions and a poor description of the histologic lesions. Cases which do not meet these requirements should not be considered proved instances of tuberculosis of the stomach. It is inter-

esting to note that in nearly half of the cases reviewed by Broders the diagnosis was considered questionable or was rejected, whereas this was true in only 2 of the 27 cases which were reported between 1929 and 1936.

The pathologic manifestations of gastric tuberculosis are varied, and their study is interesting because of the wide variety of lesions that have been described. A classification of types is difficult because of the frequency of bizarre lesions which do not fit readily into any group. The classification suggested by Biernath,¹⁴ which is as nearly complete as can be desired, is as follows: (1) simple gastritis in phthisic patients; (2) multiple small erosions and ulcers of the mucosa; (3) an ulcerating type; (4) a hypertrophic, infiltrating form; (5) a sclerosing inflammatory type; (6) acute miliary dissemination, and (7) extragastric forms of tuberculosis which involve the stomach. The first type may result in any of the other types.

There are no extensive figures available which indicate the incidence of simple gastritis among phthisic patients. Marfan¹⁵ reported gastritis in 18 of 27 cases in which necropsy was performed on tuberculous patients. The report of gastroscopic examinations performed on tuberculous patients by Rodríguez Ollerós and de la Viesca García¹⁶ likewise indicated that the incidence of gastritis is high. This type of lesion is manifested by a thickening of the gastric mucosa, by hyperemia and microscopically by round cell infiltration of the mucous and submucous layers of the stomach.

Multiple small erosions and ulcers of the mucosa are rare among phthisic patients. The most typical case of this group was that described by Hamilton,¹⁷ in which there were between 115 and 120 small erosions and ulcers which involved a considerable proportion of the gastric mucosa. The lesions are superficial; they penetrate the mucosa but never the muscularis. There is some hypertrophy of the mucous membrane, and there is considerable hyperemia. The histologic picture is that characteristic of tuberculosis, associated with the formation of tubercles and round cell infiltration. There are usually some phlebitis and endarteritis in the region of the tubercles. The perigastric lymph nodes are frequently involved. This involvement is sometimes associated

14. Biernath, P.: Zur Kasuistik der Magentuberkulose, *Deutsche med. Wchnschr.* 47:1091-1092 (Sept. 15) 1921.

15. Marfan, B. J. A., cited by Broders.⁶

16. Rodríguez Ollerós, A., and de la Viesca García, P.: El estómago tuberculoso y el estómago de los tuberculosos, *Rev. españ. de enferm. d. ap. digest. y de la nutrición* 1:745-764 (Oct.) 1935.

17. Hamilton, A.: Multiple Tuberculous Ulcers of the Stomach with a Report of Three Cases, *Bull. Johns Hopkins Hosp.* 8:75-79 (Jan.) 1897.

with general miliary tuberculosis, but according to Simmonds it frequently occurs independently of general involvement.

The ulcerating type of gastric tuberculosis is the most frequent and the most important. In the 5 cases observed at the Mayo Clinic the disease was of this type. This type occurs in about 80 per cent of all cases of tuberculosis of the stomach. In Broders' study of 305 cases it was present in 81.6 per cent of all cases in which the diagnosis was positive and in 80.5 per cent of all cases in which the diagnosis was considered probable. The ulceration is usually in the pyloric region and is more frequently on the lesser than on the greater curvature. Good reported 17 pyloric lesions in 26 cases. Ricard and Chevrier reported that in 34.7 per cent of their cases the lesion was situated at the pylorus. The pylorus is often adherent to the head of the pancreas or to the liver, the transverse colon or the duodenum. The occurrence of a gastroduodenal fistula was reported by Mathieu and Rémond.¹⁸ It is generally agreed that the high incidence of tuberculosis in the pyloric region is due largely to the number of lymph follicles in that region as compared to the rest of the stomach. Superimposition of tuberculosis on a nonspecific ulcer (which is common in the pyloric region) may likewise be a factor. Simmonds said that this is the most common origin of tuberculous ulceration.

The ulcer is usually not more than 1 to 2 cm. in diameter. However, it may be 10 by 20 cm. in diameter, which was the size of the ulcer in a case reported by Glaubitt. It is usually shallow and rarely penetrates beyond the submucosa, but instances of perforation have been reported by Kundrat,¹⁹ Marfan, Paulicky,²⁰ and Struppler.²¹ The ulcer is practically identical with that associated with intestinal tuberculosis. The edges are ragged, undermined and overhanging, and the surrounding mucosa is thickened, hyperemic and edematous. The floor of the ulcer is covered with necrotic debris and is usually gray or yellow. There is considerable peritoneal thickening in the vicinity of the ulcer. The regional lymph nodes are often caseous and necrotic.

Microscopically, there are numerous typical epithelioid and giant cell tubercles in the submucosa surrounding the ulcer, and the infection may burrow along the submucosa for a considerable distance in all directions. There is necrosis of the base and hypertrophy of the margins of the

18. Mathieu and Rémond, cited by Broders.⁶

19. Kundrat, cited by Benjamin, J.: Ueber einen Fall von lymphogen entstandenen tuberkulösem Magenschwür, *Beitr. z. Klin. d. Tuberk.* **84**:249-254, 1933.

20. Paulicky, cited by Abbott, D. P.: Tuberculosis of the Stomach, in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1923, vol. 7, pp. 511-516.

21. Struppler, T., cited by Broders.⁶

ulcer. Considerable small round cell infiltration is seen in the surrounding tissues. Endarteritis and phlebitis of regional arteries and veins are common, but the capillaries are usually dilated. There may be some lymphocytic infiltration of the muscular layers, but the infection is chiefly limited to the mucosa and submucosa. The peritoneum is thickened and congested over the ulcer.

The tuberculous granulations around the margins of the ulcer and also the healing of the ulcer may lead in the later stages to scarring and thickening of the pylorus. This transforms the ulcer into a hard cartilage-like mass which causes contraction of the pyloric ring and obstruction to the passage of gastric contents into the duodenum. Pyloric stenosis may also be produced by spasm, by perigastric adhesions or by compression of the pylorus by enlarged and caseous regional lymph nodes.

The hypertrophic infiltrating type is the second most common type of gastric tuberculosis. It usually involves chiefly the pyloric region and forms a firm, indurated mass which grossly resembles the scirrhus type of carcinoma of the stomach. In this condition the formative process is in excess of the destructive processes, and there is a great formation of tuberculous granulation tissue; the mucous membrane is folded, thickened and nodular, and it may encroach on the lumen of the pyloric region so much as to cause almost complete obstruction. Giant cells are abundant, but miliary tubercles are not common, and caseation is absent. Considerable edema and small cell infiltration of the mucosa and submucosa are present. Endarteritis and phlebitis are common. The diagnosis may be difficult unless there is involvement of regional lymph nodes. Tumor masses the size of walnuts have been described by Melchior²² and Konjetzny.²³ Beresgonowski,²⁴ Pfanner,²⁵ and von Tappeiner²⁶ have described lesions the size of eggs, and in Ruge's²⁷ case the mass was the size of a human fist.

Acute miliary tuberculosis of the stomach is relatively common; it usually is associated with general miliary tuberculosis. This lesion is

22. Melchior, E.: Tuberculosis of the Stomach, abstracted, *J. A. M. A.* 87: 888 (Sept. 11) 1926.

23. Konjetzny, cited by Pohl, R.: Ueber Tuberkulose des Magens, *Röntgenpraxis* 4:423-428 (May) 1932.

24. Beresgonowski, cited by Pohl, R.: Ueber Tuberkulose des Magens, *Röntgenpraxis* 4:423-428 (May) 1932.

25. Pfanner, cited by Pohl, R.: Ueber Tuberkulose des Magens, *Röntgenpraxis* 4:423-428 (May) 1932.

26. von Tappeiner, H.: Beitrag zur Kenntnis der tuberkulösen Pylorusstenose, *Beitr. z. klin. Chir.* 66:371-376 (March) 1910.

27. Ruge, cited by Pohl, R.: Ueber Tuberkulose des Magens, *Röntgenpraxis* 4:423-428 (May) 1932.

caused by tubercle bacilli which are poured into the blood stream from some focus of infection and which are distributed throughout the body. Miliary tuberculosis of the stomach is not of any clinical importance, since it is usually only a small factor in a rapidly fatal condition. Wilms²⁸ has reported an interesting case of this type, in which the patient was a child aged 9 months.

Extragastric forms of tuberculosis which involve the stomach occur when tuberculosis invades the stomach from neighboring organs, such as the duodenum and the pancreas or the perigastric lymph nodes.

Nedelec²⁹ called attention to a rare type of gastric tuberculosis in which "cold abscesses" of the stomach were found in the cases reported by Schlesinger³⁰ in 1914 and by Mathieu and Rémond³¹ in 1921. A solitary tubercle of the stomach is extremely rare. Van Wart³² has described an interesting case in which the tubercle was 3.5 cm. in diameter. It was situated on the greater curvature, 6 cm. from the cardia. Tuberculosis was not demonstrable elsewhere in the body; hence there was no definite evidence that this lesion was not primary in the stomach. Genkin and Sosnowik³³ in 1934 reported a case in which there were many fistulas which ended blindly in the thick wall of a tuberculous stomach. These authors called particular attention to the thrombosis of the blood vessels around the fistulas. The route of infection in this case was apparently by retrograde lymphatic spread from tuberculous hilar nodes to the perigastric lymph nodes.

In brief, tuberculosis of the stomach may appear in any stage from acute fulminating to chronic infiltrating forms, and the diagnosis must usually be made by histologic examination.

RELATION OF GASTRIC CARCINOMA AND TUBERCULOSIS

The association of carcinoma and tuberculosis in the same body or organ has been a subject of considerable interest and controversy among pathologists for many years, and extensive literature has accumulated regarding this subject. At present the weight of evidence, as voiced by

28. Wilms, M.: Miliartuberkulose des Magens, *Centralbl. f. allg. Path. u. path. Anat.* 8:783-789 (Sept.) 1897.

29. Nedelec, M.: La tuberculose de l'estomac, *Arch. franco-belges de chir.* 34:76-104 (Feb.) 1934.

30. Schlesinger, H., cited by Knoflach and Pape.¹²

31. Mathieu and Rémond, cited by Abbott, D. P.: Tuberculosis of the Stomach, in Tice, F.: *Practice of Medicine*, Hagerstown, Md., W. F. Prior Company, Inc., 1923, vol. 7, pp. 511-516.

32. Van Wart, R. M.: Solitary Tubercle of the Stomach, *Bull. Johns Hopkins Hosp.* 14:235-237 (Sept.) 1903.

33. Genkin, S., and Sosnowik, J.: Klinik und Pathologie einiger Formen der Magen- und Lebertuberkulose, *Virchows Arch. f. path. Anat.* 292:315-321 (April) 1934.

Menniti,³⁴ Schacter,³⁵ Broders,³⁶ and Cooper,³⁷ supports the contention that tuberculosis and carcinoma in the same body or organ are not antagonistic. This contention certainly is borne out in the case of tuberculosis and carcinoma of the stomach. To date a total of 368 cases of gastric tuberculosis have been reported in the literature, and of these not more than 60 per cent can be classed as positive or probable cases of gastric tuberculosis according to the criteria postulated by Broders. An analysis of these same cases revealed that in 30 of the 368 cases gastric tuberculosis and gastric carcinoma were coexistent. This incidence of association is rather high, certainly higher than occurs in most organs of the body in which these conditions can coexist. Perhaps this can be accepted as evidence in support of the theory that cancer, ulcer and erosion of the gastric mucosa may lower its resistance to tuberculous infection and act as portals of entry for infection. Certainly, this incidence of associated lesions seems too high to be explained entirely by coincidence.

The first case of associated gastric tuberculosis and carcinoma was reported by Clement³⁸ in 1895. Since then, 28 additional cases of coexisting gastric tuberculosis and carcinoma and 1 case of associated sarcoma and tuberculosis have been reported. In 5 cases the carcinoma was considered primary; in 3 cases tuberculosis was believed to have developed first. No opinion was stated in the other cases. In 12 cases there was definite evidence of pulmonary tuberculosis.

These cases of associated gastric tuberculosis and carcinoma are interesting chiefly as pathologic curiosities. It is generally agreed that there is nothing about the history or clinical findings that is of any particular value as regards the diagnosis, and the treatment is always surgical.

DIAGNOSIS

At the outset it must be said that there is no way in which a definite clinical diagnosis of tuberculosis of the stomach can be made. There are no characteristic signs or symptoms, and there is no laboratory test or group of tests that can indicate to the observer the nature of the disease. The difficulty lies largely in the fact that the symptoms and signs resemble, or are identical with, those of pathologic gastric condi-

34. Menniti, M.: Sull'associazione di tubercolosi e neoplasie maligne, *Pathologica* **25**:180-190 (March 15) 1933.

35. Schacter, cited by Cooper.³⁷

36. Broders, A. C.: Tuberculosis Associated with Malignant Neoplasia: Report of Twenty Cases, *J. A. M. A.* **72**:390-394 (Feb. 8) 1919.

37. Cooper, F. G.: The Association of Tuberculosis and Carcinoma, *Am. Rev. Tuberc.* **25**:108-147 (Jan.) 1932.

38. Clement, G.: Ueber seltene Arten der Combination von Krebs und Tuberculose, *Virchows Arch. f. path. Anat.* **139**:35-58, 1895.

tions infinitely more common than gastric tuberculosis. Gastric tuberculosis closely resembles gastric ulcer, gastric carcinoma and gastric syphilis and must sometimes be distinguished from tumor of the pancreas, carcinoma of the gallbladder, benign tumor of the stomach, pylorospasm and hypertrophic pyloric stenosis. The problem is further complicated by the fact that patients frequently may have two or more of these conditions in the stomach at the same time. It is true of tuberculosis of the stomach, as of most rare diseases, that the diagnosis is not made because the condition is not thought of, and the rarity of the condition makes this only natural. However, the disease has been diagnosed clinically in 6 instances, by von Schlesinger, Haudek,³⁹ Spengler,⁴⁰ Pohl,⁴¹ Lapeyre,⁴² and Pop and Hanganutiu,⁴³ and it is one of the purposes of this paper to call the attention of clinicians to this condition so that it may be considered more frequently in the differential diagnosis of gastric disease.

Gastric tuberculosis usually affects young adults; it rarely affects persons beyond 35 years of age, but in some cases which have been reported the patients were adults who were 60 and 70 years of age, and in others they were children who were less than a year old. It occurs among male patients approximately twice as frequently as among female patients. The onset is usually insidious, but the course is steadily progressive. The symptoms most frequently noted are loss of appetite and a sense of epigastric fulness and pressure after meals, especially if solid food has been eaten. There may be a burning, gnawing pain which comes on two or more hours after meals and is relieved by the ingestion of food. As the condition progresses, vomiting develops, and there is pain in the upper part of the abdomen, which often is cramplike. This pain is usually relieved by vomiting. As the vomiting grows progressively worse the vomitus becomes stagnant and frequently contains food which was eaten several meals previously. The patient gradually loses strength and weight. Occasionally, hematemesis occurs. Arloing noted hematemesis in 9 of the 147 cases he reported. Benjamin⁴⁴ reported that

39. Haudek, cited by Knoflach and Pape.¹²

40. Spengler, cited by Knoflach and Pape.¹²

41. Pohl, R.: Ueber Tuberkulose des Magens, *Röntgenpraxis* 4:423-428 (May) 1932.

42. Lapeyre, L. N.: Ulcère tuberculeux de l'estomac: Une observation complète: clinique, anatomique, histologique, *Gaz. méd. de France (suppl. Gastroenterol.)*, March 1, 1933, pp. 3-6.

43. Pop, A., and Hanganutiu, M.: Klinische und röntgenologische Betrachtungen über die Tuberkulose des Magens, *Zentralbl. f. Chir.* 59:1629-1635 (July) 1932.

44. Benjamin, J.: Ueber einen Fall von lymphogen entstandenem tuberkulösem Magengeschwür (Tödliche Hämatemesis), *Beitr. z. Klin. d. Tuberk.* 84: 249-254, 1933.

fatal hematemesis occurred in the cases reported by Bignon,⁴⁵ Kundrate, Brechemin,⁴⁶ Long,⁴⁷ Plate,⁴⁸ and Reinhold,⁴⁹ and in 1 case of his own. Diarrhea, which appears early and continues throughout the course of the disease, is rather characteristic, but constipation occurs not infrequently, as has been pointed out by Curschmann.⁵⁰ A history of pulmonary tuberculosis may be entirely lacking.

Physical examination usually reveals that the patient is pale and thin and appears ill. There may or may not be evidence of pulmonary tuberculosis. The stomach is often dilated, and occasionally its outline can be made out without difficulty. Visible peristalsis is common, and it may be possible to elicit a succussion splash. There is usually considerable epigastric tenderness, and in 50 per cent of cases there is a palpable mass in the pyloric region. Usually the mass is firm, well defined and movable. A daily variation of temperature is highly suggestive of tuberculosis.

As mentioned previously, laboratory data do not offer anything pathognomonic of gastric tuberculosis. There is usually some anemia, and this may be striking, but diagnostically it cannot be relied on. Analysis of the gastric contents is not conclusive but does offer some information. As has been shown by Cohen⁵¹ and others, the acidity of the gastric contents in persons with tuberculosis of the stomach is much lower than it is among normal healthy persons. In the large majority of cases of gastric tuberculosis the acidity of the gastric contents is decreased, and complete anacidity is not uncommon, as it occurred in the cases reported by Alessandri,⁵² Alexander,⁵³ Fujii⁵⁴ and others. In Lee's⁵⁵ case no free hydrochloric acid was observed even after injection of histamine, which usually has the property of stimulating the secretion of acid. On the other hand, in cases which were reported by Curschmann and Schlesinger there was hyperchlorhydria. There may be occult

45. Bignon, cited by Benjamin.⁴⁴

46. Brechemin, G., cited by Lusena, G.: *Stenosi pilorica da granuloma tuberculare*, Arch. ital. di chir. 4:1-31, 1921.

47. Long, cited by Benjamin.⁴⁴

48. Plate, cited by Benjamin.⁴⁴

49. Reinhold, H., cited by Benjamin.⁴⁴

50. Curschmann, H.: *Klinischer Beitrag zur Tuberkulose des Pylorus*, Beitr. z. Klin. d. Tuberk. 2:127-140 (June) 1904.

51. Cohen, S. J.: *Study of Gastric Function in Pulmonary Tuberculosis*, Nat. Tuberc. A. Tr. 28:184-186 (June) 1932.

52. Alessandri, cited by Broders.⁶

53. Alexander, M.: *Beitrag zur Tuberkulose des Magens*, Deutsches Arch. f. klin. Med. 86:212-216 (Dec.) 1906.

54. Fujii, R., in Kaufmann, E.: *Lehrbuch der speziellen pathologischen Anatomie für Studierende und Ärzte*, Berlin, W. de Gruyter & Co., 1922, vol. 1, pp. 528-529.

55. Lee, F. C.: *The Surgery of Tuberculosis of the Pylorus*, Am. Rev. Tuberc. 26:323-368 (Oct.) 1932.

blood in the gastric contents, but the finding of tubercle bacilli in the secretions may be of slight significance. Examination of the stools rarely gives much information. Even the finding of occult blood in the stools is of little significance, as it may be due to the hemophthysis of pulmonary tuberculosis or to any number of other gastrointestinal conditions. The urine is practically always normal. The injection of tuberculin has been advocated by some as a diagnostic method. It cannot be used as a routine test, because of the danger of a severe reaction or even of perforation. This test is mentioned only to be condemned.

Roentgenologic investigations are of considerable value in determining the presence or absence of a gastric lesion, but they rarely contribute much of a definitely diagnostic nature, since the roentgenogram of the lesion is almost identical with that produced by more common gastric lesions, such as carcinoma and ulcer. Roentgenologists of great experience can frequently differentiate between a carcinomatous lesion and a granulomatous lesion such as occurs with tuberculosis or syphilis, but there are no definite criteria for the differentiation of these two lesions. With the ulcerating type of gastric tuberculosis, which makes up 80 per cent of the lesions, the roentgenologic picture is that of a nonspecific gastric ulcer, with perhaps a little more scarring and contracture than occur with the ordinary ulcer. The hypertrophic, infiltrating type produces nonspecific pyloric stenosis, which simulates that produced by either carcinoma or syphilis of the stomach. Renander⁵⁶ has described a cufflike infiltration with equal contours and a uniform circular shadow as being characteristic of gastric tuberculosis. Rother⁵⁷ noticed a slight break between the bulb and the canal and believed this finding was of considerable significance. Haudek has called attention to the uniform narrowing of the pylorus. Schmitz⁵⁸ has postulated that if infiltration extends into the duodenum one should suspect tuberculosis, as carcinoma never extends into the duodenum. Pop and Hanganutiu were impressed by the smooth, amputated appearance of the pylorus in a case of tuberculosis of the stomach observed by them, as compared with the irregular outline common in cases of carcinoma of the stomach. There is usually some evidence of pulmonary tuberculosis, and it should always be searched for. Leriche⁵⁹ found roentgenologic evidence of pulmonary tuberculosis in all but 2 of a series of 24 cases of tuberculous gastric ulcers. Roentgenologic evidence of osseous or intestinal tuberculosis would be suggestive. Roentgenologists are agreed that it is impossible to make a diagnosis of gastric tuberculosis from the roentgenologic appearance at a single examination.

56. Renander, A.: Einige röntgenologisch Beobachtete Fälle von Magentuberkulose, *Acta radiol.* **11**:636-648, 1930.

57. Rother, cited by Renander.⁵⁶

58. Schmitz, cited by Pop and Hanganutiu.⁴⁵

59. Leriche, R., cited by Pohl.⁴¹

Lee's dictum that when the patient is an adult 20 to 40 years of age with signs of pyloric obstruction, diarrhea, fever, a movable pyloric mass and pulmonary tuberculosis, one should suspect gastric tuberculosis, holds good for a majority of cases, but it should be extended to include any person who has a digestive disturbance and evidence of tuberculosis anywhere in the body.

PROGNOSIS

In considering the prognosis of gastric tuberculosis one cannot regard the disease as a clinical and pathologic entity confined to the stomach. Gastric tuberculosis is a complication of an infectious process with foci elsewhere in the body. It is doubtful if a case of proved primary gastric tuberculosis has ever been reported, although a number of cases have been reported as such. According to the statistics of Glaubitt and Blas,⁶⁰ tuberculosis of the stomach is associated with pulmonary tuberculosis in 94 to 100 per cent of cases, with intestinal tuberculosis in 69 to 91.5 per cent and with tuberculosis of the liver and the lymph nodes in 74 and 68.1 per cent, respectively.

The only satisfactory treatment of tuberculosis depends on rest, fresh air, sunshine and adequate nutrition. Interference with or lack of any of these elements is immediately harmful. Gastric tuberculosis occurs only as a complication of an already existing tuberculous process, and striking as it does at one of the keystones of tuberculosis therapy, adequate nutrition, it rapidly endangers the life of the afflicted person. The loss of appetite, digestive disturbance, vomiting and diarrhea so often produced by gastric tuberculosis result in a loss of strength and weight and a degree of dehydration that are extremely dangerous to the patient already weakened by tuberculosis. Return of normal gastric function must be brought about promptly or the lowered resistance of the patient will permit an extension of the primary tuberculous focus, which may be fatal. Restoration of gastric function can be brought about only by surgical methods. If possible, the infected portion of the stomach should be removed. If this is not possible, continuity of the gastrointestinal tract must be restored by means of a gastroenterostomy, which allows nutrition to be maintained with as little interference as possible. Gastric operations in cases of tuberculosis are extremely difficult and dangerous. The frequent coexistence of a tuberculous process involving the transverse colon, the duodenum, the liver, the pancreas and the regional lymph nodes further complicates this perplexing surgical problem. The possible development of tuberculous bronchopneumonia as a result of the anesthesia or of shock incident to the operation constitutes a considerable hazard. Even so, the prognosis is infinitely better with operation than without.

60. Blas, M., cited by Lee.⁵⁵

TREATMENT

The treatment of gastric tuberculosis still leaves much to be desired, although with improvements in diagnostic methods patients are seeking treatment before the tuberculous process has extended too far for satisfactory treatment. It must be admitted that too few patients who have gastric tuberculosis are given the benefit of a correct clinical diagnosis. However, medical treatment has little to offer, and surgical treatment must always depend on what is found at exploration; therefore, the patient has little to lose if a diagnosis of a surgical gastric lesion is made and prompt surgical attack is carried out. Good's dictum that surgical treatment be prescribed for almost all chronic gastric lesions does not seem too radical.

In all cases of gastric tuberculosis reported up to 1889 the lesions were observed at necropsy. In that year Ricard and Chevrier performed the first surgical operation in a case of gastric tuberculosis. An anterior gastroenterostomy was performed. This case stimulated Ricard and Chevrier to review the literature on gastric tuberculosis, and in their report they reached the following conclusion in regard to treatment: "The knowledge of the pathologic anatomy of the causal lesions imposes the abandonment of certain varieties of intervention. Resection is useless because impossible, and if attempted would be dangerous." Gastroenterostomy was generally accepted as the treatment of choice until 1902, when Koerte⁶¹ performed the first resection of the stomach for gastric tuberculosis. A Billroth II type of resection was done.

The surgical procedure carried out should usually be dictated by the findings on exploration. Gastric resection is the treatment of choice whenever possible, and gastroenterostomy should be used only when the patient is in bad condition or when resection is contraindicated by extensive involvement of other abdominal viscera, generalized peritoneal involvement or severe intestinal tuberculosis. Knoflach and Pape collected 58 cases in which resection was performed. Good results were obtained in 36 of these cases. Lee collected 80 cases in which gastric tuberculosis involved the pylorus. In 51 cases gastroenterostomy was performed, and in 19 resection was the procedure carried out. Forty-five per cent of the patients who were subjected to gastroenterostomy were well after the operation. Sixty-five per cent of the patients who underwent gastrectomy were well after the operation. In all 5 cases observed at the clinic the patients have been treated by resection.

After all, the type of operation preferable is not a matter which merits too much consideration, as the operation must depend on the pathologic process present and on its extent. In general, resection should be performed for any chronic, well localized type of gastric tuberculosis

61. Koerte, cited by Nedelec.²⁹

in which there is not a generalized involvement of the abdominal cavity or viscera, extensive pulmonary tuberculosis or a general physical condition contraindicating a prolonged operative procedure. Gastroenterostomy usually should be performed whenever resection is not justified. Other types of surgical procedure, such as pyloroplasty and gastroduodenostomy, are rarely indicated.

SUMMARY

Tuberculosis of the stomach is a comparatively rare gastric lesion. Only 368 cases have been reported in the literature. The disease may occur at any age but is most common in persons of 35 to 45 years. Males are affected twice as frequently as are females. Infection of the stomach usually occurs by way of the blood stream but may occur by way of the lymphatics, by direct infection of the mucosa and by direct continuity or contiguity of structure. There is no completely satisfactory explanation of the relatively high immunity of the stomach to tuberculosis. The chief pathologic types of gastric tuberculosis are: (1) the ulcerating type; (2) the hypertrophic infiltrating type; (3) acute miliary dissemination; and (4) extragastric forms involving the stomach. The ulcerating type is present in at least 80 per cent of cases. In approximately 10 per cent of cases of gastric tuberculosis the disease is associated with carcinoma. There is no proof of antagonism between carcinoma and tuberculosis. The coexistence of the two conditions in the stomach seems too high to be entirely coincidental, but no reasonable explanation for this association has been suggested. Clinically, tuberculosis of the stomach closely simulates peptic ulcer, gastric carcinoma and gastric syphilis. Only rarely can the diagnosis be made before histologic examination of the gastric lesion. A positive diagnosis of gastric tuberculosis can be made only by the demonstration of the tubercle bacillus in the lesions. The treatment of gastric tuberculosis should always be surgical. Resection of the involved portion of the stomach is the operation of choice whenever possible.

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PATHOGENIC BACTERIA IN THE AIR OF OPERATING ROOMS

THEIR WIDESPREAD DISTRIBUTION AND THE METHODS OF CONTROL

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In a preliminary publication¹ I have shown the presence of pathogenic bacteria (predominately *Staphylococcus albus* and *Staphylococcus aureus*) in the air of the operating rooms of the Duke Hospital. Various regulations for reducing the numbers of these bacteria were described, the most important of which follow:

1. Rigid isolation was practiced. No visitors were permitted; the personnel of the operating room was kept as small as possible, and no one was allowed to enter the rooms when they were not in use.

2. Large, heavy masks were worn over the nose and mouth by all occupants at all times, regardless of whether an operation was in progress.

3. All persistent carriers of *Staph. aureus* in the nose and throat were excluded, and important operative procedures were postponed when the contamination of the air was high.

4. Scrupulous cleanliness was maintained by frequent washing and painting and by eliminating air currents from other parts of the hospital.

5. The concentration of bacteria in the air was diluted by "washing out" the room continuously during occupancy with a large amount of air, which was taken from outside the building, where there were few if any pathogenic bacteria, and was rendered practically free of non-pathogenic fungi, spores and gram-negative bacilli by washing and filtering in the air-conditioning system.

In spite of all these precautions, there were rises in the contamination of the air with pathogenic bacteria associated with an increase in

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1. Hart, D.: Operation Room Infections: Control of Air-Borne Pathogenic Organisms, with Particular Reference to Use of Special Bactericidal Radiant Energy. *Arch. Surg.* 34:874-896 (May) 1937.

the number of carriers during and following epidemics of infection of the respiratory tract. In order to anticipate these periods of increased risk of infection, daily cultures of the air in the operating rooms were made. It was usually possible to identify the organism on the culture plate exposed to the air during an operation before the same organism was recovered from the wound in the occasional case in which infection occurred.

A method of controlling this contamination of the air by the use of bactericidal radiation was described in the preliminary report.¹ It was shown that Petri dishes of blood agar sprayed with the hemolytic *Staph. aureus* and exposed at the operative site could be sterilized within from one to three minutes and that at this point the number of bacteria dropping out of the air could be reduced by from 95 to 100 per cent. This intensity of radiation will not give the patient an appreciable burn during an exposure of ninety minutes.²

As I anticipated, it was soon stated by some physicians that this contamination of the air was a local condition and that no pathogenic bacteria were present in the air of their operating rooms. Approximately fifty surgeons in twenty-five states were asked to make cultures in the operating rooms in which they worked, in order to determine the extent and degree of this contamination of the air. Reports were received from thirty-two surgeons.³ These covered thirty-seven operating rooms in thirty-three hospitals located in seventeen states. The reports are summarized in the table and demonstrate conclusively the widespread, if not universal, presence of pathogenic bacteria in operating rooms during occupancy.

All cultures, unless otherwise designated, were made by exposing a Petri dish of blood agar to sedimentation from the air for one hour during an operation at points 5 feet (150 cm.) and 7 feet (215 cm.) from the operative incision and 3 feet (90 cm.) above the floor. These were incubated for forty-eight hours; photographs were taken and the colonies identified (figs. 1-4). The number of occupants and the duration of occupancy before exposure were given in most reports. The state was given in all reports except one, in which it was specifically requested that the name be withheld. The table is incomplete in many respects, but this could not be avoided since there were wide variations in the reports sent in from the different hospitals.

Because of the size of the table, important facts which are demonstrated might be overlooked. To emphasize the more important points,

2. With reasonable care it is never necessary to expose any tissue for longer than this, even in an operation lasting for several hours. In 750 operations no special precautions were taken to protect the wound, and no patient received a burn.

3. All names of doctors and hospitals have been omitted, since this was the request of the majority.

reference numbers I to X are given at the left side and the bottom of the table, and these points will be considered in the order given.

I. Exclusive of bactericidal irradiation, air conditioning is the most important single means of reducing the bacterial content of the air in the occupied operating room (figs. 1 and 2). This reduction is brought about in two ways:

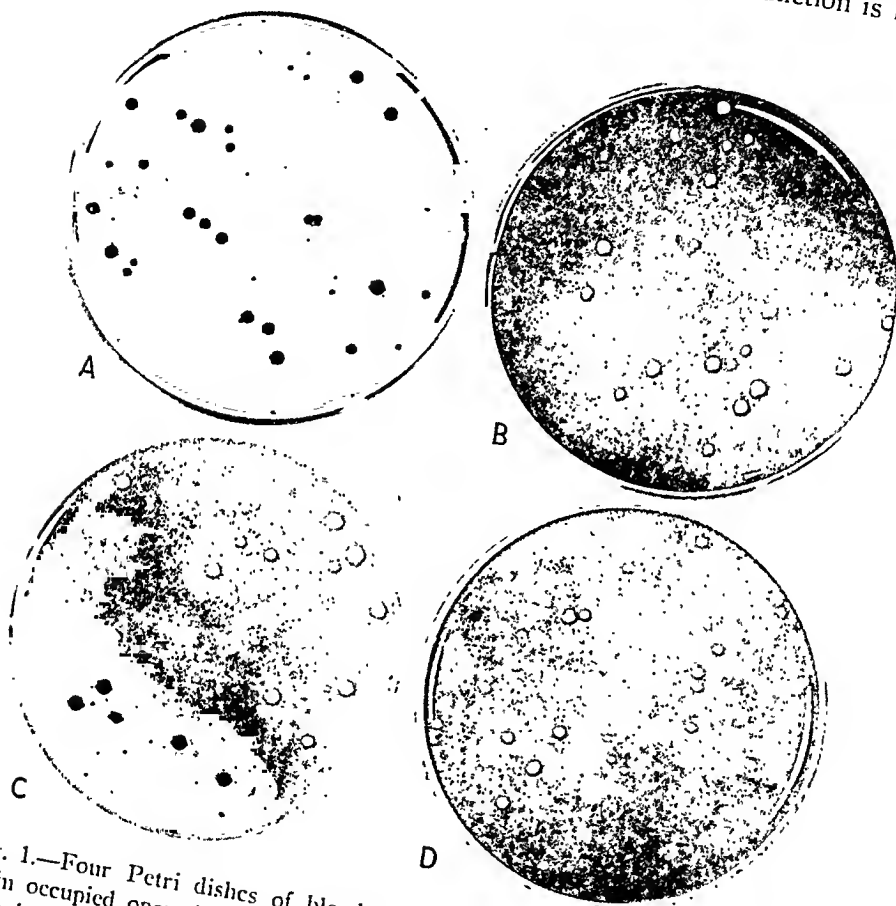


Fig. 1.—Four Petri dishes of blood agar exposed for one hour in four hospitals in occupied operating rooms which were supplied with washed and filtered air (incubated forty-eight hours): *A*, North Carolina, hospital 1 (table); *B*, Illinois, hospital 2; *C*, New York, hospital 1; *D*, New York, hospital 2. It should be noted that a large percentage of these colonies are staphylococci, with few gram-negative bacilli and practically no fungi, since these have been removed by the air-conditioning system (fig. 3). (The bacterial count and identification are given in the table.) This figure may be compared with figure 2 which illustrates cultures made in operating rooms without air conditioning. The total number of colonies of pathogenic bacteria is relatively low, since many of the organisms had been removed from the room by efficient ventilation.

(a) The organisms in the outside air (predominantly nonpathogenic, spores, gram-negative bacilli and fungi) are removed by the air-conditioning system (fig. 3).

Personal Communications Showing the Presence of Pathogenic Bacteria in

	State	Hospital Number	Dates of Exposures	Average Number of Occupants	Duration of Occupancy Before Making of Culture	Number of Exposures	Average Number of Colonies per Plate*	Staphylococcus			
								Aureus		Albus	Citreus
								Hemo-lytic	Nonhemo-lytic		
I	Illinois.....	1	10/22/36	5+	60 min.	12	—	1	9	—	—
	Illinois.....	2	11/ 4/36	8	60 min.	1	26	—	—	15	—
	Illinois.....	3	10/27/36	9	210 min.	1	67	4	5	35	—
	New York.....	1	9/26/36	16	68 min.	7	21	0	1.1	15	—
	New York.....	2	11/ 4/36	9	4	36	0	3	22	8.5
	North Carolina	1	9/10/36 10/ 1/36	11	120 min.	10	22.5	0.4	1	18	0.1
II	Massachusetts.	2	9/30/36 10/ 7/36	?	?	6	137	23	25	53	—
	Massachusetts.	2	9/30/36 10/ 7/36	?	?	4	58	7	15	32	—
	South Carolina	1	10/ 7/36	—	4	50	0	0	30	—
	South Carolina	1	10/ 7/36	—	4	38	0	0	25	—
III	Massachusetts.	1	9/30/36 (Room A) 10/ 7/36	?	?	2	34	5	16	12	—
	Massachusetts.	1	9/30/36 (Room B) 10/ 7/36	?	?	2	36	8	5	23	—
	Massachusetts.	1	9/30/36 (Room C) 10/ 7/36	?	?	2	33	16	8	8	—
	Massachusetts.	1	9/30/36 (Amphitheater) 10/ 7/36	?	?	4	119	26	25	60	—
	Massachusetts.	1	9/30/36 (Amphitheater) 10/ 7/36	?	?	2	32.5	9	12.5	10.5	—
	Texas.....	2	10/ 9/36 11/ 6/36	55 to 130	31 min.	7	100+	+	+++	++++	—
V	Virginia.....	1	10/28/36	9	30 to 60 min.	10	93	5	37.1	35	—
	Alabama.....	1	9/24/36	9	?	2	188	—	—	—	—
	Alabama.....	2	9/24/36	6	0 min.	2	100	—	—	+	—
	Connecticut....	1	10/29/36 11/ 6/36	12	53 min.	6	54	—	4	39	—
	Indiana.....	1	11/../36	7	40 min.	1	82	0	0	0	0
	Iowa.....	1	2/11/37	7	60 min.	2	81	0	0	41	—
VI	Kansas.....	1	10/19/36	8 to 10	60 min.	2	100++	+	+	+	—
	Maryland.....	2	9/28/36	7	60 min.	16	60	(+?)	+? 33	++++	(+)
	Maryland.....	1	10/../36	—	2	54	0	0	12	—
	1	10/ 7/36	12	180 min.	1	115+	++++	+++++	+++	—
	Minnesota.....	1	10/19/36 (Room A)	13	Several hours	2	67	10	+	+	—
	Minnesota.....	1	10/21/36 (Room B)	11	60 min.+	2	60	21	+	+	—
VII	Missouri.....	1	11/14/36	8	4	—	0	0	+	+
	New York.....	3	10/ 9/36	9.5	3 min.	2	56	0.5	3.5	39.5	—
	North Carolina	2	10/ 1/36	6	2	104	5.5	6	39.4	—
	North Carolina	3	9/27/36	7	120 min.	1	35	2	0	33	—
	North Carolina	4	10/15/36 10/20/36	5.5	120 min.	4	42	0.5	4	35	—
	North Carolina	5	11/14/36	7	?	3	66	16	14	34	—
	Ohio.....	1	10/12/36	7+	45 min.	6	45	1.5	2	34	—
	Tennessee.....	1	10/10/36	10	180 min.	5	66	+	+	+	—
	Tennessee.....	2	10/ 8/36	9	120 min.	1	90	5	31	45	—
	Texas.....	1	10/ 1/36 10/23/36	7	120 min.+	12	43	0	8	22	—
	Texas.....	3	11/../36	?	—	—	(..	34	..	—
	Virginia.....	2	11/ 4/36	—	3	171	(..	18)	41	—
							VII	VIII			

* The number of colonies per pour of exposure was much lower in the air-conditioned than in the nonair-conditioned cases.

Relatively Large Numbers in Every Hospital Where Cultures Were Taken

Streptococcus		Fungus	Bacillus Subtilis	Diphtheroid	Others	Comment
Hemo- lytic	Nonhemo- lytic					
—	—	—	—	—	2	Operating; air washed and filtered
—	1	—	—	—	9	Operating; air washed and filtered
1	—	2	—	—	19	Operating; air washed and filtered
0	0	0.5	0.5	3	1	Operating; air conditioned
—	—	1	1.5	—	0.5	Operating; air conditioned
—	—	1.5	1.5	0	0	Operating; air conditioned
0.5	0.5	—	—	—	35	Operating; occupied
0.2	1	—	—	—	2.5	Not operating; unoccupied
0	0	0.5	—	—	19	Operating
0	0.25	0.5	—	—	8	Not operating
0.5	0	—	—	—	1	Operating
0.5	0	—	—	—	—	Operating
0	0	—	—	—	2	Operating
1	3	—	—	—	4	Operating
0.5	0	—	—	—	—	Operating; cultures of supply table covered with sterile canopy open at front
—	—	++++	++++	—	++++	Operating; not all colonies identified
0	13.5	—	—	—	3.1	Operating; four occupants suffering from colds
—	—	—	—	+	—	Operating
—	—	—	—	—	—	Operating
0	0	—	—	—	11	Operating
0	0	0	0	0	0	Operating
0	1.5	—	—	—	35.5	Operating
0	0	+	—	—	+	Operating
0	0	+	+	+	+	Operating; not all colonies identified
0	0	12	2	24	3	No note as to occupancy
—	—	—	—	—	+	Operating; three wounds infected with Staph. aureus during exposure of plates (three weeks)
0	0	—	—	—	—	Operating; not all colonies identified
0	0	—	—	—	—	Operating; not all colonies identified
0	0	+	—	+	+	Operating; colonies not counted; not all colonies identified
0	0.5	—	0.5	5	—	Operating; not all colonies identified
2	—	—	—	—	51.5	Operating
0	0	—	—	—	—	Operating
—	—	—	—	—	3	Operating
0	0	1	—	—	—	Operating
—	0.2	—	—	—	8	Operating
0	0	+	—	+	—	Operating; not all colonies identified
—	—	—	—	—	6	Operating
0.33	0	—	—	—	13	Operating
—	—	—	—	—	—	Operating; colonies not counted; not all colonies identified
—	—	14	(..)	77	20	Operating

IX

X

(b) The organisms given off in the room by the occupants (predominantly pathogenic, staphylococci and occasionally streptococci) are removed more rapidly by the clean, circulating air from an efficient ventilating system.

II. Other things being equal, the number of pathogenic bacteria in the air of a room increases directly with the number of occupants and

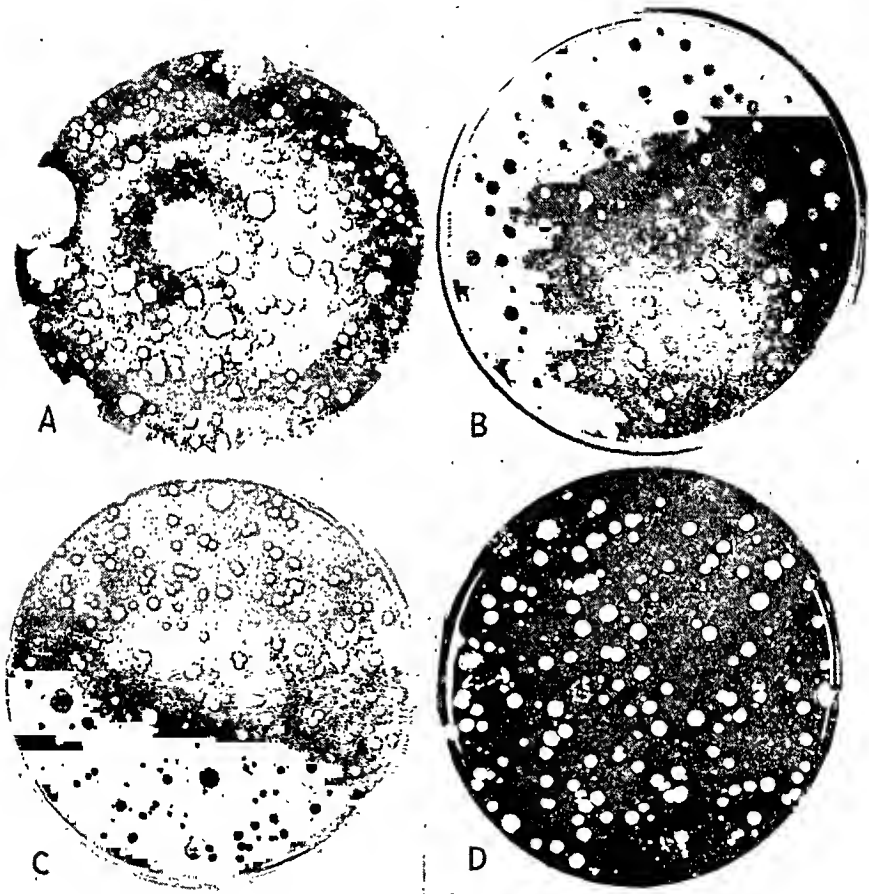


Fig. 2.—Four Petri dishes of blood agar exposed for one hour in four occupied operating rooms which were not supplied with washed and filtered air (incubated forty-eight hours): *A*, Kansas, hospital 1 (table); *B*, Massachusetts, hospital 1; *C*, Texas, hospital 2; *D*, Virginia, hospital 2. Since the gram-negative bacilli, spores and fungi in the outside air have not been removed (fig. 3), they are mixed with the pathogenic bacteria given off by the occupants of the room. The pathogenic bacteria are also in greater concentration than in the room supplied by an efficient ventilating system. (The bacterial count and identification are given in the table.) This figure may be compared with figure 1.

the duration of occupancy. Conversely, the bacterial count drops directly in proportion to the length of time the room is unoccupied and closed.

I have shown this also in previous publications⁴ and have demonstrated repeatedly that the air in an operating room that has been closed for from fifteen to twenty hours is almost free of bacteria. In such a room few viable organisms can be stirred up by air currents from electric fans directed against the floor.

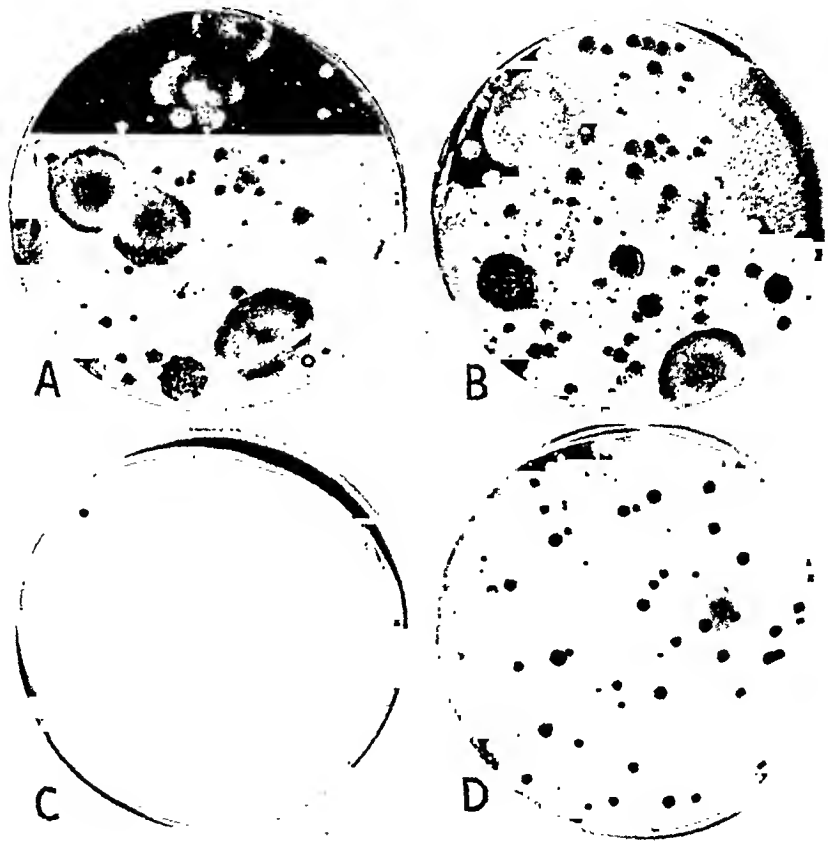


Fig. 3.—Removal of bacteria from the air by washing and filtering and contamination of the clean air by the occupants of the room. The dishes were exposed simultaneously for one hour (A) at the intake for the ventilation system on the roof of the hospital, (B) in the washing chamber of the decontaminating system, (C) at the opening of the supply air duct in the occupied operating room, and (D) at the opening of the exhaust air duct in the occupied operating room and incubated for forty-eight hours at 37.5 C. It has been shown by streak culture that the relatively nonpathogenic bacteria and fungi present in the outside air are removed by washing and filtering but that the air entering the operating room is quickly contaminated with staphylococci. (Hart, D.: *Sterilization of the Air in the Operative Region with Radiant Energy*, Tr. South. S. A. [1936] 49:376-401, 1936.)

4. Hart, D.: Sterilization of Air in Operating Room with Radiant Energy, J. Thoracic Surg. 6:45-81 (Oct.) 1936.

III. A room with many occupants has a much higher bacterial count than an adjoining room with few occupants (fig. 4). This fact I have demonstrated repeatedly, and the situation is what would be expected if the pathogenic bacteria are given off by the occupants of the room.

IV. A canopy over the sterile supply tables is of some value in cutting down the contamination of these supplies. This has been demonstrated by Truesdale⁵ and probably by many others. It seems unwise to allow sterile supplies to be exposed to sedimentation of bacteria for longer than one operation, and even during that time they should receive every protection that can be given.

V. Only one report made any reference to the prevalence of infections of the respiratory tract. With four occupants of the operating room

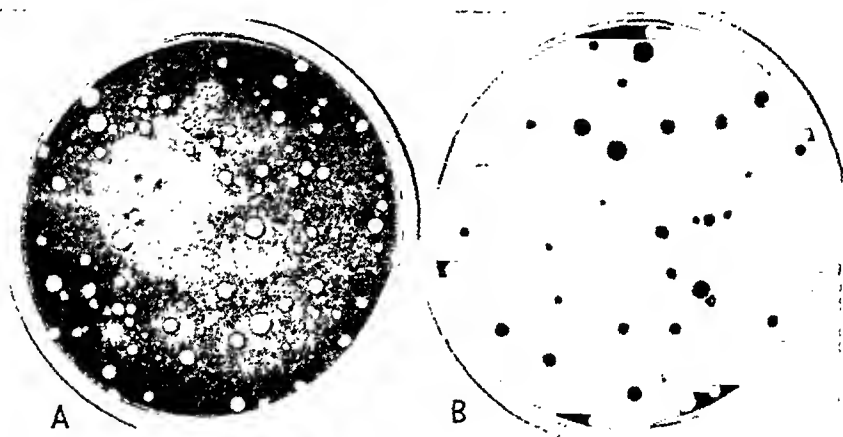


Fig. 4.—Petri dishes of blood agar exposed for one hour at the same time of the year in the same hospital (not supplied with washed and filtered air): (A) in the amphitheater, Massachusetts, hospital 1 (table), and (B) in a small operating room, Massachusetts, hospital 1, and incubated for forty-eight hours. There are three times as many colonies of bacteria on the Petri dish exposed in the amphitheater as on that exposed in the smaller adjoining operating room, which had relatively few occupants.

suffering from colds, the Petri dishes of blood agar exposed for one hour showed an average of 13.8 colonies of streptococci per Petri dish. Only this report stated an appreciable number of the organisms were in the air. It is my opinion that in an epidemic of infection of the respiratory tract, during which the beta hemolytic streptococcus is present in many noses and throats, these organisms reach the wound and the sterile supplies by way of the air and cause the familiar flare-up in the incidence of infections. I have shown that the concentration of *Staph. aureus*

5. Truesdale, P. E.: Operating Room Safeguards, *Mod. Hosp.* 23:19-21 (July) 1924.

in the air of the operating rooms at Duke Hospital is proportional to the number of carriers present.¹

VI. During the three weeks covered by the test, with heavy sedimentation of *Staph. aureus* from the air (cultures made in hospital 1 in a state whose name was omitted by request), three wounds were infected with this organism. For over two years I made daily cultures of the air in an attempt to anticipate any considerable rise in the contamination of the air with *Staph. aureus*, hemolytic or nonhemolytic. During the peaks of contamination of the air with this organism the danger of infection of wounds was definitely increased.

VII. The total number of colonies of bacteria sedimenting from the air gives some idea of the degree of contamination of the air⁶ but is of less significance than the number of pathogenic organisms present. In this respect air conditioning, by removing most of the nonpathogenic organisms from the incoming air and only diluting the concentration of the pathogens in the room, gives more apparent than actual improvement in operating conditions. This statement is not intended to discredit air conditioning, which I consider extremely valuable for reducing the concentration of the pathogenic organisms in the air and for eliminating the danger of infection from contaminated perspiration.

VIII. The majority of the pathogenic bacteria reported were staphylococci. I have found that at times these organisms are present in the noses and throats of a high percentage of the population. The large number of carriers, together with the resistance of the organism to drying, probably accounts for this preponderance. The air as a medium for transportation of these organisms to the wound has never received due consideration, probably for two reasons: 1. It has been said that the air can be ignored as a source of infection of wounds. 2. Because of the universal presence of these organisms on the skin, such infections of wounds are usually ascribed to poor technic in handling the skin. In my experience over 90 per cent of infections of wounds are caused by staphylococci. I am convinced that in most cases the infection is caused by dropping of the organisms in the air into the wound or on the sterile supplies that will enter the wound.

IX. Streptococci were recovered from the air in relatively small numbers. This may probably be accounted for by the relatively few carriers and the susceptibility of the organism to drying. The organism is probably present in the air of the operating room in large numbers during epidemics of infection of the respiratory tract, when this organism is present in many of the noses and throats. Infections of wounds

6. From my experience it is fair to assume that in general the number of colonies reported from these cultures made during the fall are fewer than would be the case if the cultures had been made during the winter.

have been traced to carriers of streptococci. Because of the high incidence of streptococcic infections of wounds, many operating rooms were closed except for emergency cases during the influenzal epidemic of 1918, at which time a large proportion of the population were carriers of streptococci. I feel that at such times the streptococci most likely reach the wound and sterile supplies by way of the air.

X. The group which includes all organisms other than staphylococci and streptococci is incomplete, since in many reports no attempt was made to identify and count the relatively nonpathogenic organisms.

In the Duke Hospital, by sterilizing the air with bactericidal radiation, it has been possible to get an operative field from which less than one colony per Petri dish per hour of exposure can be cultured. With this technic unexplained infections in primary clean incisions have practically disappeared. The postoperative course is far smoother; the elevation of temperature is much less and of shorter duration; there is less soreness in the wound, and the general systemic reaction is much less than when radiation is not used.

CONCLUSIONS

Pathogenic bacteria floating in the air and universally present in the occupied room are the greatest cause of infection in clean incisions in the modern, well run operating room.

While air conditioning with forced ventilation is effective in reducing the amount of contamination of the air, it is highly desirable that the remaining organisms in the vicinity of the wound and the sterile supplies be killed.

Bactericidal irradiation offers the most effective method of sterilizing the air at the present time and should be used to protect the region of the operation and the sterile supplies until some equally efficient and more desirable method is made available.

ACUTE OSTEOMYELITIS OF THE LONG BONES OF ADULTS

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NEW YORK

Orthopedic surgeons are familiar with acute osteomyelitis in children. It is a clinical entity so clearcut that the diagnosis in a typical case may be made with reasonable certainty. Nevertheless, in spite of the pioneer work done in an attempt to educate the general practitioner to consider its possibility, acute osteomyelitis is still treated under the mistaken diagnosis of rheumatism or rheumatic fever. It is, I think, the most poorly treated of all conditions requiring surgical treatment, and great damage is caused by delay in instituting surgical drainage.

In the reports of cases of acute osteomyelitis, authors have frequently included cases of adults, and some have called attention to the fact that in these cases there was a "difference" in the onset and in the subsequent course. No one has had a large experience with such cases, and inquiry discloses the fact that physicians who have treated many patients with acute osteomyelitis have never observed a case in which the condition first appeared after active growth had ceased. Indeed, Robertson¹ stated: "This disease is to be found in its primary attack only up to the age at which the last epiphysis unites. It never occurs after fusion of the epiphysis."

The literature on acute osteomyelitis is enormous. I have found no article on the picture presented when the onset occurs in adult life. Indeed, I have found only one article, by Prass,² related to my subject; it covered primary osteomyelitis in the aged, obviously an extremely limited field.

The history of acute osteomyelitis in childhood is characteristic. The child is extremely ill. There is often preceding trauma, such as contusion or sprain, to the affected parts, and the onset of symptoms occurs twenty-four or forty-eight hours later. There is usually a preceding or concomitant cutaneous infection or sore throat. The patient complains of excruciating pain located near the end of a long bone.

Read before the American Orthopedic Association at Lincoln, Neb., June 2, 1937.

1. Robertson, D. E.: Acute Septic Osteomyelitis, *M. J. Australia* 2:66, 1925.

2. Prass, E.: Ueber primäre Altersosteomyelitis, *Deutsche Ztschr. f. Chir.* 236:644, 1932.

The temperature is elevated, ranging from 104 to 106 F., and there may be associated chills.

The patient is examined cautiously, and it is found that the neighboring joint is not involved. There is local sensitiveness at the site of infection in the bone, usually in the position of the metaphysis. The skin and the subcutaneous tissue may show slight edema and a pinkish tinge if the involved area of bone is superficial and the condition has existed for forty-eight hours or more. Cellulitis is not present at this stage. The white blood cell count is elevated to about 20,000, and the percentage of polymorphonuclear leukocytes is increased to 85 or 90.

I have reviewed the records of 9 cases of acute osteomyelitis of the long bones of adults. Five of the patients in these cases were treated by me and 4 by three other surgeons. Seven of these were men and 2 were women. Compound fracture and the sclerosing osteomyelitis of Garré were not included. The following data were obtained at the time of admission to the hospital:

Patient	Sex	Age	Weeks After Onset	Rectal Tempera- ture, F.	White Blood Cell Count	Polymorpho- nuclears, Percentage
J. L.	M	39	3	100	10,600	67
C. F.	M	32	3	104	29,200	94
L. C.	M	38	1½	103.4	17,750	86
W. H.	M	22	6	99.6	10,400	76
P. W.	F	32	1½	101.8	13,000	78
D. T.	M	45	6	104	22,800	87
I. R.	M	60	4	100	8,900	65
A. L.	M	31	3	99	10,600	72
M. M.	F	19	20	99	8,000	52
Average			5½			

ETIOLOGY

There was a history of trauma in 3 cases. There was no possibility of trauma in the other 6 cases. One patient dropped a case of beer on his thigh three weeks before the pain brought him to the hospital. The second dropped a heavy can, containing some liquid substance, on his ankle three weeks before he was seen by me. The third struck his thigh against a stepladder three weeks prior to seeking relief for the pain. There was no preceding infection or illness in 6 cases, sore throat in 1 case, mammary abscess following lactation in 1 case and phlebitis following parturition in 1 case.

The onset in children is fulminating. In adults the progress of the disease is slow and insidious but of gradually increasing intensity. (However, at times the onset in adults follows the pattern seen in children.) What is responsible for the difference in manifestation of acute osteomyelitis in the child and in the adult? If cases of compound fracture are omitted from consideration, there must be a positive blood culture at some stage in all cases of acute osteomyelitis, even though no organisms may be observed when culture is made. This is mentioned

here because many physicians and even surgeons feel that a positive blood culture represents an additional complication, whereas, since the lesion is metastatic, such a manifestation is a part of the picture at some stage of the disease.

PATHOLOGY

The pathologic changes are principally central and periosteal. The involved portion of the central canal is filled with granulation tissue and pus.

If the lesion has existed for a long time this central granulation tissue becomes more fibrous.

The disease may have its origin in the former metaphysial region, as is observed with children. It is more likely to be in the shaft, since there is a more evenly distributed supply of blood to the bone in adults than in children, whose vascular activity is concentrated in the region of greatest growth.

The route of spread in the long bones of the adult is principally through the central canal, and the changes are more evident in the marrow cavity than in the osseous substance.

The development of subperiosteal abscess in adult bone is unlikely, though pus may be localized about an area in which there is periosteal involvement. This is due to the more firm adherence of the periosteum to the cortex in fully grown bone, and the accepted theory of spread advanced by Choyce³ and modified by Starr⁴ does not apply.

When the involvement is near the end of the bone in the cancellous substance there is a tendency to invasion of the neighboring joint. When new periosteal bone is produced it is light in texture and may be peeled off the outer part of the cortex readily. There may be pus formed about this area of periostitis. Eventually, after operation, the bone is restored to a relatively normal appearance, there being little gross distortion other than that incidental to operation.

The disease may be localized in the medullary cavity without the usual diffuse involvement seen in childhood.

There may be a local area of periosteal bone production with pus formation intimately associated with barklike thickening on the surface of the shaft. There may seem to be but little evidence of further disease. Indeed, in 1 case I drained an abscess localized about the shaft of the femur and could not convince myself that the shaft should be opened, so slight was the reaction. Later I opened the medullary cavity for a considerable distance and found it filled with pus and granulation tissue.

3. Choyce, C. C.: *A System of Surgery*, London, Cassell & Co., 1912-1915.

4. Starr, C. L.: *Acute Hematogenous Osteomyelitis*, *Arch. Surg.* 4:567 (May) 1922.

Sequestrum formation in these cases (I do not include cases of recurrence in which the onset was in childhood) must be an uncommon occurrence. In only 1 case was there a sequestrum necessitating removal, and it was small.

The lesion may be in the shaft of the bone or at the end. The bone most likely to be involved is the femur, and the diseased area, the shaft.

Starr concluded that the lesion usually has its onset in the metaphysical region and that when the medullary cavity is involved it is by backward extension through the haversian system.

It is likely that trauma in the adult is as common as in the child. The invading bacteria, one may assume, are the same; therefore, the difference in location and spread of the disease is influenced by the difference in the architecture of the bones of adults and children.

In children the vascular channels are more numerous, particularly near the ends of the long bones. When the growth disk disappears, the channels on the two sides of the barrier become continuous, and vascular activity in this region is diminished.

Of 9 cases the culture showed *Staphylococcus aureus* in 7 and *Streptococcus haemolyticus* in 1. In the remaining case no organisms could be demonstrated at the time of operation, five months after onset. The infecting organisms had disappeared from the marrow cavity, though histologic evidence of chronic inflammation remained. The diagnosis in this case was not made until operation was performed five months after the onset. The characteristics of the disease in adults and in children may be summarized as follows:

	Children	Adults
Onset.....	Acute; fulminating	Gradual
Pain.....	Excruciating from the onset	Marked but not well localized; increasing in intensity
Temperature and white blood cell count	Very high	Usually moderately elevated
Preceding infection and trauma	Usually present	Usually absent
Roentgen findings.....	Early picture normal; after several weeks extensive involvement, with sequestrums	Early picture normal; after several weeks involvement relatively localized, without sequestrums
Method of extension....	From metaphysis through haversian system, subperiosteal abscess	Not through haversian system, no subperiosteal abscess

SYMPTOMS

Pain is the most constant symptom. It is less severe than that in children, though it is often intense. The temperature during the early days or weeks is either normal or slightly elevated. The white blood cell count in the early stage is but slightly elevated, and the increase in the percentage of polymorphonuclears is usually slight. Later the temperature may be high, reaching 104 F. or more, and the white blood cell count and the percentage of polymorphonuclears may be propor-

tionately increased. The lesion often assumes chronic characteristics before the correct diagnosis is made, even though the patient may have been under the observation of competent physicians. Less frequently the onset is fulminating.

In the early stages roentgen examination shows no abnormality; the pathologic picture appears more gradually than with children, requiring several weeks to several months for outstanding evidence of disease to be shown. The lesion is localized. There is spotty atrophy of the cortex over an area of several inches, and there is associated production of periosteal light bone over the same area if the shaft is involved. There may be destruction of the cortex presenting as an area of local erosion. At the ends of the bones one sees only spotty atrophy. The new periosteal bone produced has a laminated appearance at times and may be confused with an endothelioma. One does not encounter the extensive involucrums that are seen in children. At times roentgenograms have suggested a sequestrum, but in only 1 case did one develop.

DIAGNOSIS

The most important point in the diagnosis of osteomyelitis is to consider the possibility of its existence. One must not be too strongly influenced by the presence of a low blood cell count or by the absence of fever. Absence of local trauma does not militate against the diagnosis. With a complaint of intense local pain over a bone, considered to be genuine, and with corresponding local sensitiveness without evidence of other disease or involvement elsewhere in the body, one must suspect acute osteomyelitis. An increase in this intense, boring pain in spite of palliative remedies entitles the patient to an exploratory operation.

TREATMENT

There is a tendency among certain surgeons toward a "laissez faire" attitude even with children, based on the hope that there will be localization of an abscess which may be drained. I do not approve of this attitude. When one has seen acute osteomyelitis in a child a few hours after the onset and has operated on the child, drilling the bone, and the lesion has healed without sequestrum formation, one contrasts that picture with another observed two weeks after onset, in which three fourths of the shaft is involved and the child is subjected to a number of subsequent operations, with hospitalization and added expense, before complete healing ensues. The same thought occurs when one finds involvement of one bone neglected and multiple foci in other bones occurring as a sequel. There seems to be no tendency to metastatic involvement from the original bone focus in adults. One must remember that acute osteomyelitis is a serious condition and that death may

result from an overwhelming infection. The treatment employed by me in all cases has been the Orr method, which is the most comfortable and economical for the patient. It requires the least amount of hospitalization. The operative procedure for adults should be the removal of a window of cortex about 1 or more inches (2.5 cm.) long and $\frac{1}{2}$ or $\frac{3}{4}$ inch (1.3 to 2 cm.) wide instead of the simple drilling carried out for children. The only objection to Orr's method is the odor that is present during convalescence. This is offset by its many advantages.

REPORT OF CASES

CASE 1.—J. L., a man aged 39, was first seen at the Mount Vernon Hospital on Jan. 19, 1935, complaining of pain in the left thigh and leg. Three weeks previously he had "turned" the left leg and felt some pain in the region of the knee. At this time he also dropped a case of beer on the left foot. The pain continued. There was no redness, heat or swelling.

Examination showed that the patient was not ill. The rectal temperature was 100 F. The pulse rate was 75, and the white blood cell count was 10,600, with 67 per cent polymorphonuclears. There was sensitiveness indefinitely located about the left thigh on the medial and the lateral aspect. There was no discoloration or infiltration. The circumference of the two thighs was identical. The roentgenogram showed no abnormality. After two days the patient was discharged. The temperature had varied from 99.4 to 100.8 F. It was my impression that he had rheumatism.

He returned to the hospital on January 29 because the pain had increased. He was sensitive to deep pressure over the lower third of the left femur. There were no signs of infection of the soft parts. The temperature was 99 F. The white cell count was 15,600, with 85 per cent polymorphonuclears. The sedimentation rate was 18 mm. in twelve minutes.

The roentgenograms taken at the time of this admission showed slight production of new periosteal bone with cortical involvement affecting the femoral shaft near the junction of the middle and lower thirds (fig. 1).

I operated on the patient two days after the second admission. The affected area was found to consist of new, heaped-up periosteal bone of slight degree with perhaps a drachm (3.7 cc.) of thick pus about it. This was drained. I could not convince myself that the bone should be opened. Culture of the pus showed *Staph. aureus*.

No relief was obtained, and on February 3 I explored the femur through a long lateral incision. At this time the temperature was 103.2 F. A drill hole just above the external condyle showed pus. Another drill hole 8 inches (20 cm.) higher revealed pus in the medullary cavity. The lateral wall of the femur was removed, leaving a trough 8 inches (20 cm.) long. The cortex was found softened. The medullary cavity was found filled with pus and granulation tissue. The Orr treatment was carried out.

At the time of the second operation the knee joint was found distended. It was deemed wise not to open it.

The first dressing was done on February 26. The wound was found filled with clean red granulation tissue.

The temperature remained irregularly elevated. Numerous blood cultures yielded *Staph. aureus*. The patient received five transfusions, and when he left the hospital, on April 22, the wound was healing. There was undoubtedly invasion

of the knee joint. He was walking with crutches. The knee was relaxed and painful. He was given a long caliper brace.

On July 25 he was readmitted to the hospital for a third time, and he remained under observation for a few days. The temperature was normal.

When the patient was seen in the clinic in January 1936, the left knee showed slight local elevation of temperature, but there were no other inflammatory signs. The knee could be flexed to 90 degrees and extended to 180 degrees. The brace had been discarded, and the patient was comfortable and working.

CASE 2.—C. F., a man aged 32, was first seen at the Mount Vernon Hospital Sept. 19, 1930, because of pain in the left ankle. The onset was insidious. The



Fig. 1.—Acute osteomyelitis of the left femur, showing localized destruction and periostitis.

temperature was 104.6; the pulse rate was 120; and the white blood cell count was 29,200, with 94 per cent polymorphonuclears. Three weeks previously a large can containing liquid had fallen on the patient's left ankle. At the time of admission the pain in the left ankle was intense. The patient was acutely ill.

Examination showed the left ankle to be swollen and red. There were local heat and fluctuation in front of the malleoli. There was extreme sensitiveness in this region.

The roentgenogram showed no essential abnormality. A diagnosis of acute osteomyelitis was made, and the patient was operated on immediately after the examination. The ankle was opened through several incisions. Four ounces (120 cc.) of thick pus was evacuated. Through and through drainage was established. The

top of the astragalus was found denuded as was the lower end of the tibia, including its articular surface. The culture yielded *Staph. aureus*.

The urine showed numerous casts and red blood cells. Blood cultures showed *Staph. aureus*.

The patient was given transfusions without avail. The temperature after operation declined gradually. It remained at 102 F. for several days. Prior to death it rose abruptly to 108 F. Death occurred on September 28.

CASE 3.—L. C., a man aged 38, was admitted to the Mount Vernon Hospital on July 4, 1935. Nine days previously he had had a sore throat. He had had fever at this time and had been kept in bed for three days. On the day of onset the patient had a chill and noticed pain in both thighs. The pain in the right leg continued. The pain in the left leg subsided spontaneously. The pain was in the thigh. It did not radiate. It was dull, aching and constant. It was made worse by movement of the extremity.

Examination showed the patient to be in good condition. The right thigh was swollen just above the midportion. In this region, for 4 or 5 inches (10 or 12 cm.), on the lateral aspect, there was sensitiveness to deep pressure. The soft parts were tense, but picking them up between the examining fingers did not cause pain. There were no enlarged glands in the groin. The knee and the hip were normal. The temperature was 103.4 F. The white blood cell count was 17,750, with 89 per cent polymorphonuclears. A diagnosis of acute osteomyelitis of the right femur was made, and immediate operation was advised. The patient would not consent.

Roentgenograms showed a slight elevation of the periosteum below the lesser trochanter.

On July 5 the patient was operated on. The thigh was explored through a long lateral incision. The superficial muscle fibers were red and normal. The deeper fibers of the vastus externus were pale. After the structures had been split down to the bone, pus was encountered, and 4 ounces of thick pus was evacuated. At this time a pure culture of *Str. haemolyticus* was obtained. The periosteum was found injected. It was friable and peeled back easily. Several drill holes were made into the medullary cavity. The cortex was softened and white, but no pus exuded from the holes. The wound was packed with petrolatum gauze, and over the dressings a plaster of paris bandage was applied from the toes to the groin. A blood culture was negative.

The patient's temperature gradually returned to normal, and his further course was uneventful. When he was last seen on November 12, his recovery was complete.

CASE 4.—W. H., a man aged 22, was first seen by me at the Mount Vernon Hospital Oct. 24, 1933. He complained of pain in the right arm of six weeks' duration. The pain was growing progressively worse. There was no preceding illness or injury. He had lost 9 pounds (4.1 Kg.) since the onset. There were no chills or fever. The pain was localized in the midportion of the arm.

Examination showed him to be in poor condition. There was a fusiform swelling of the right arm just above the midpoint. There was no local heat in this region, but there was sensitiveness over the midportion. The skin was not adherent. There was no infiltration of the soft parts. The temperature was 99.6 F. The white blood cell count was 6,200, with 77 per cent polymorphonuclears. The sedimentation time was fifty minutes.

Roentgen examination showed an area of rarefaction 2 inches (5 cm.) long, involving the middle third of the humerus. There was involvement of the medul-

lary canal but no expansion of the shaft. Slight periostitis was evident about the lesion. A Wassermann test of the blood was negative. The urine showed no Bence-Jones protein. The diagnosis lay between localized osteomyelitis and endothelioma.

Further roentgenograms were taken, which showed progression of the elements noted in the original films (fig. 2). The films were submitted to a group of physicians interested in tumors of the bone, who felt that irradiation, which had been started, should be continued; they advised definitely against operation.

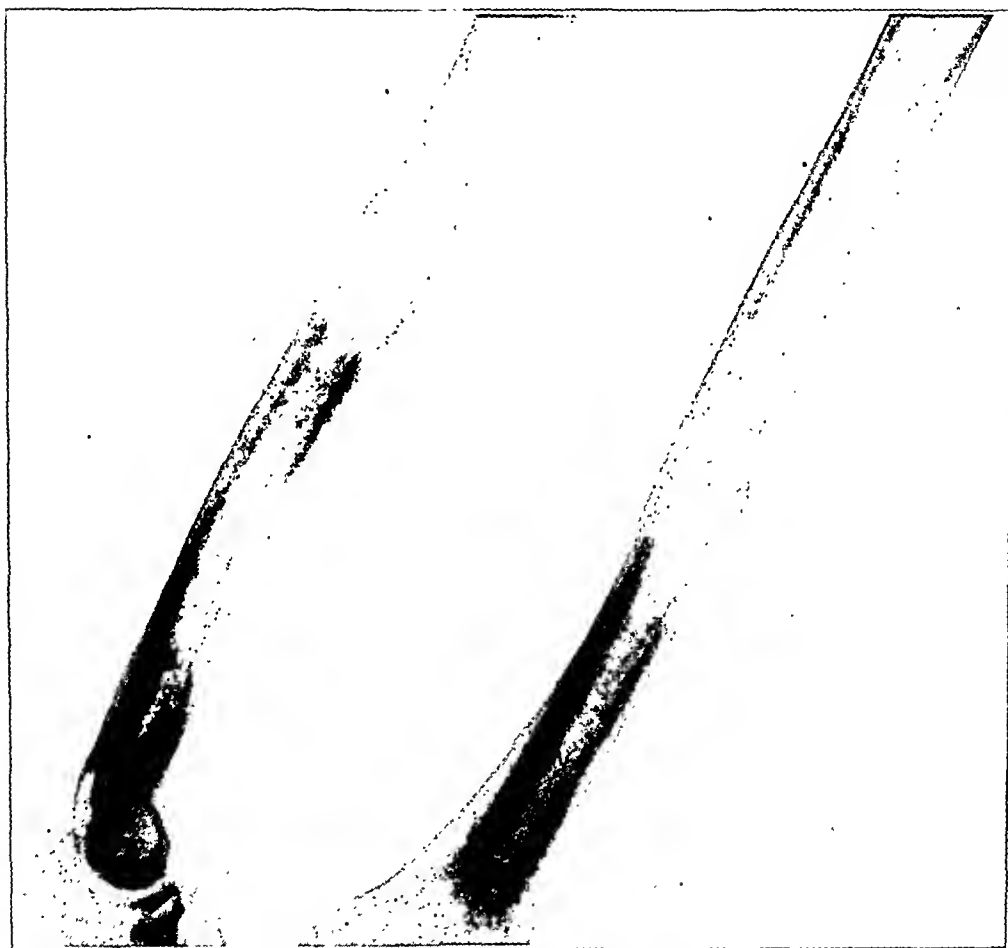


Fig. 2.—Acute osteomyelitis of the right humerus, showing local destruction with localized periostitis.

The patient's temperature became slightly elevated and reached 101.6 F. The circumference of the right arm was $9\frac{3}{8}$ inches (22 cm.) on admission; three weeks later the circumference was $10\frac{3}{8}$ inches (25 cm.). On this date the white blood cell count was 10,400, with 64 per cent polymorphonuclears.

The patient's pain, which became more severe, was not completely relieved by opiates.

On November 6 the humerus was explored. The periosteum was found thickened, and pus was present about it. The cortex of the bone was softened. A window was cut from the humerus in the affected area. Pus and granulation tissue were found in the medullary cavity. Drill holes were made into the medullary cavity above and below this window, which was $1\frac{1}{2}$ inches (4 cm.) long, and $\frac{1}{2}$ ounce (14.8 cc.) of thick pus was evacuated. The Orr method was used.

Culture of the pus showed a pure growth of *Staph. aureus*.

The patient was last seen on Jan. 28, 1934. At this time he had no symptoms referable to the arm. Examination showed cardiorenal disease with incipient decompensation. Efforts to trace him later were unsuccessful.

CASE 5.—P. W., a woman aged 32, was seen Sept. 26, 1931, because of pain in the right knee. The patient had been delivered of a child on July 14. The labor was uncomplicated. Six weeks later an abscess developed in one of the breasts. This was incised and drained. On September 10 she complained of pain in the right knee. An excess of fluid was found in the knee at this time. The rectal temperature was elevated to 101.8 F. The pain and swelling subsided in the knee but later recurred.

When the patient was seen by me, the right knee was swollen. It was in full extension and could be flexed to 70 degrees. There was an excess of fluid in the knee joint, especially in the quadriceps pouch. There was sensitiveness generally about the knee, especially about the femoral condyles (and particularly the medial condyle). The temperature was 103 F. The pain was acute and was localized at the knee.

Roentgen examination of the knee and the lower half of the femur showed no abnormality. The white blood cell count was 13,000, with 78 per cent polymorphonuclears. Morphine did not relieve the pain.

On September 30 aspiration was done, and turbid fluid was removed from the knee. The puncture wound was sealed with collodion, and the lower end of the femur just above the medial condyle was explored. The periosteum was reddened and injected. It was split, but no pus was encountered. Drill holes were made into the cancellous bone in this region, and at a depth of $1\frac{1}{2}$ inches (4 cm.) thick, creamy pus was encountered. It was under tension and was pulsating. A window was cut into the cortex above the inner condyle; the wound was packed with petrolatum gauze, and plaster of paris was applied.

Culture from the pus showed a pure growth of *Staph. aureus*.

On October 8 it was necessary to drain the knee through a lateral incision. Four ounces (118.3 cc.) of thin pus was evacuated. Culture of this pus also showed *Staph. aureus*. The wound was packed loosely with petrolatum gauze, and four Carrel tubes were sewed into it. An aluminum splint was applied posteriorly.

The patient was given several transfusions. The further course was uneventful, and she made a complete recovery, a normal range of motion in the knee being restored.

CASE 6.—D. T., a man aged 45, a dentist, was first seen by Dr. Samuel Jahss on March 17, 1931. The onset had occurred six weeks previously, with pain in the right groin. There had been no preceding illness or injury. There were sharp pain, fever and chills. At this time the white blood cell count was 22,800, with 87 per cent polymorphonuclears.

Roentgen examination, on March 22, of the right hip and femur showed no abnormality.

Roentgen examination of the same area on March 31 showed mottling of the upper third of the femur, with medullary destruction extending from the greater trochanter down the shaft for 3 inches (7.5 cm.). There was slight cortical involvement (fig. 3).

Culture of the blood on a number of occasions showed *Staph. aureus*.

On March 23 operation was performed and drainage instituted for what was thought to be gluteal myositis. The patient was given a number of transfusions.

Roentgenograms of April 4 showed more extensive involvement, with some periosteal new bone.

On April 13 the shaft of the right femur was saucerized from the tip of the greater trochanter downward through two thirds of the shaft. The upper third



Fig. 3.—Acute osteomyelitis of the right femur, showing spotty atrophy of the upper portion of the shaft.

of the medullary cavity was found filled with pus and granulation tissue. The Orr treatment was carried out, a plaster of paris spica being used.

Culture of the pus showed *Staph. aureus*. The patient was readmitted to the hospital several times for dressings and new plaster of paris spicas.

CASE 7.—I. R., a man aged 60, was first seen by Dr. Samuel Jahss on June 12, 1934, in the outpatient department of the Hospital for Joint Diseases. He complained of a dull ache above the right knee, which had been present for four weeks. Just prior to the onset he struck the right knee against a ladder. The "aching"

followed, continuing day and night. At first he did not pay much attention to it. He used home remedies but obtained no relief. The pain increased so much that he could not sleep. The throbbing became severe.

Examination showed the right knee to be flexed. The lower end of the femur was thickened. There was local sensitiveness to pressure on both the medial and the lateral aspect of the lower third of the femur. The inguinal glands were not enlarged. The temperature on admission was 100 F. The white blood cell count was 8,900, with 65 per cent polymorphonuclears. The temperature rose to 102.4 F.

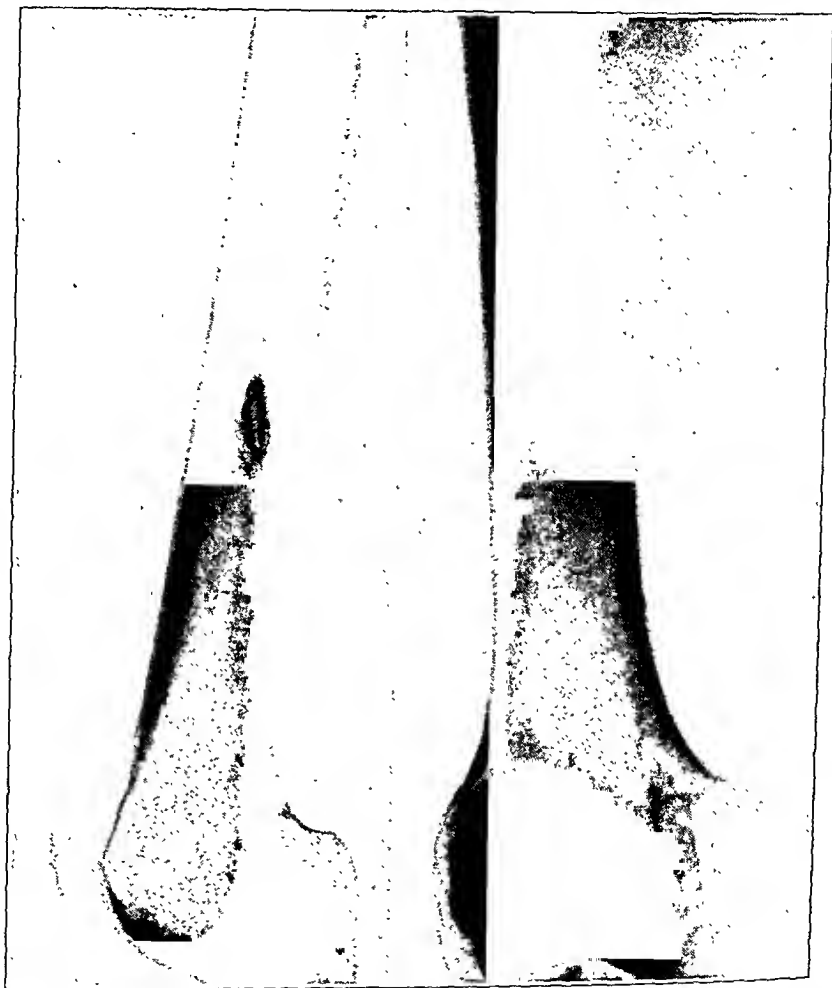


Fig. 4.—Osteomyelitis of the right femur, showing local destruction with sequestrum and periostitis. These roentgenograms were made in the only case in which a sequestrum was found.

Roentgen examination showed an ovoid osseous abscess 4 inches (10 cm.) above the lower end of the femur. In the cavity was a small sequestrum (fig. 4). There was light periostitis about the involved area. Operation was planned for the next day but was deferred because of a mild infection of the respiratory tract.

Operation was performed June 27. The femur was exposed at its lower end on the medial and the lateral side. Eight ounces (240 cc.) of pus was evacuated

when the deep muscles were split. The cortex was found roughened. The marrow cavity was found filled with pus and granulation tissue. Culture of material from the femur showed a pure growth of *Staph. aureus*. The opening into the bone was seen in the roentgenogram to be filled with granulation tissue. A small sequestrum was found in the cavity. The shaft was opened for 4 inches (10 cm.) and the wound was packed with petrolatum gauze. Plaster of paris was applied from the groin to the ankle. After a few days the plaster of paris bandage was removed, and Russell skin traction was applied because of a pathologic fracture. Carrel tubes were inserted. Diluted solution of sodium hypochlorite was instilled into the wound. There was considerable bleeding from the wound, apparently from granulation tissue. The wound had become contaminated by maggots. On July 19 the petrolatum gauze packing was reinserted. On August 8 pockets of pus about the wound were evacuated.

Roentgen examination on July 7 showed an oblique fracture of the femur at the junction of the middle and the lower third, with overriding. The bone in the affected area showed the spotty atrophy of infection in both fragments.

Blood culture on July 25, 1934, showed *Staph. aureus*. On July 31 the white blood cell count was 19,200, with 54 per cent polymorphonuclears.

Roentgenograms of August 2 showed extension of the osseous involvement into the fragments of bone. The alignment was fair.

The patient was given numerous transfusions, but he lost ground. He died on August 18 of sepsis and bronchopneumonia.

CASE 8.—A. L., a man aged 31, was first seen by Dr. John B. Stevens, of Syracuse, N. Y., on Aug. 12, 1935, complaining of pain in the upper part of the right thigh. He had noticed sudden pain in the right thigh three weeks previously, when diving from a raft. He thought he had sprained his leg. He described the pain at the time of examination as boring and constant. It was worse at night. It was not increased by active use of the leg. At this time he had no fever. The physical examination showed no abnormality except tenderness to deep pressure at the junction of the upper and the middle third of the thigh. There was no local swelling, nor were there any inflammatory signs. He had lost 10 pounds (4.5 Kg.). The hip and the knee joint were free. The temperature was 99 F., and the white blood cell count was 10,600, with 72 per cent polymorphonuclears.

The roentgenogram showed spotty involvement of the femoral shaft at the junction of the middle and the lower third, with destruction of bone and light local new periosteal bone formation (fig. 5).

Operation was performed Aug. 14, 1935. An area of rough, sclerotic bone was encountered. As this was removed, a drachm (4 cc.) of pus was evacuated. A gutter was cut into the femur. The wound was packed with petrolatum gauze. Culture of the pus yielded *Staph. aureus*.

The postoperative course was uneventful.

CASE 9.—M. M., a woman aged 19, was first seen by Dr. Harry Finkelstein Dec. 28, 1936, at the Hospital for Joint Diseases, complaining of pain in the right hip. She stated that she had gone through a normal gestation and had been delivered of a small baby on August 9. Three days after delivery she noticed severe pain in the right hip, for which she was treated with a baking lamp. (The records of the hospital stated that she had postpartum phlebitis in the right groin.) She had fever at this time, the temperature rising to 103 F. and remaining elevated for a week. She was discharged from the hospital where she had been confined after two weeks, but she had to go to bed at home because of the pain. She remained in bed for

five weeks. She sought relief from the pain and entered another hospital, where she remained for three weeks. Roentgenograms were taken and other tests were carried out. She was told she had a "hole in the bone" but was given no treatment. When she went home she was forced to go to bed.

Examination on admission to the Hospital for Joint Diseases showed that the right knee and hip were flexed. The hip was in slight outward rotation. It could be flexed to 90 degrees and extended to 150 degrees. It could be abducted to 25 degrees and adducted to 30 degrees. No internal rotation was permitted.

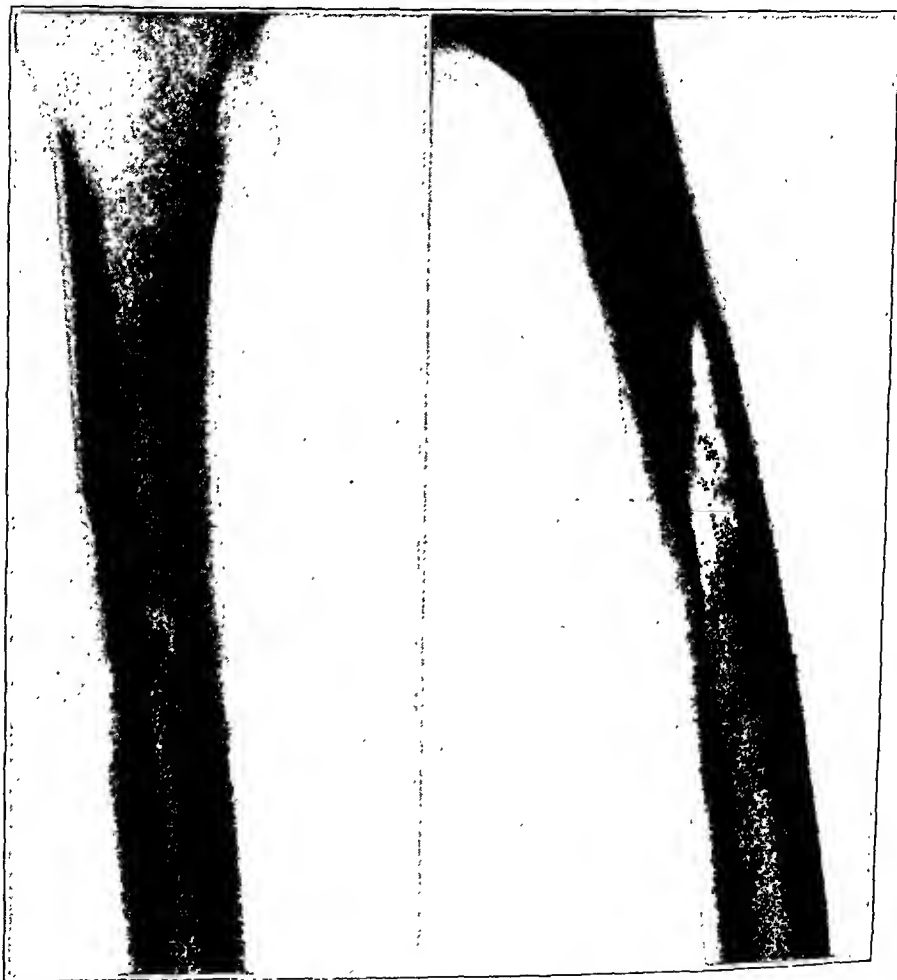


Fig. 5.—Acute osteomyelitis of the right femur, showing destruction and new localized periosteal production of bone.

A roentgenogram taken on December 30 showed the joint space of the hip to be narrowed. There was osteoperiostitis in the proximal third of the femur, associated with spotty areas of rarefaction.

The temperature on admission was 99 F. The white blood cell count was 8,000, with 52 per cent polymorphonuclears. The temperature later rose to 102 F. on occasion but for the most part remained at about 100 F. The white blood cell count on Jan. 19, 1937, was 11,400, with 65 per cent polymorphonuclears. The

sedimentation time was fifty-two minutes on Dec. 28, 1936, and thirty-four minutes on Jan. 19, 1937, the normal value being forty-five minutes.

Operation was performed on February 4. The upper end of the right femur was exposed through a lateral incision. A large window was cut in the greater trochanter. No pus was found. The bone was softened. Material for culture was sent to the laboratory, as was the specimen of bone. The wound was closed without drainage. The culture showed no growth. The specimen of bone showed that the marrow was fibrosed and infiltrated by chronic inflammatory cells. There were large vascular channels in the marrow. Dr. H. L. Jaffe's diagnosis was chronic nonsuppurative osteomyelitis.

SUMMARY AND CONCLUSIONS

1. Acute osteomyelitis of the long bones of adults presents a picture different from that usually seen in children.

2. The onset is insidious, and development of the lesion is gradual in all but exceptional cases.

3. The pain is not so acute as in children and not so well localized. Pain is the most constant symptom and usually after many days or weeks is extremely acute.

4. The roentgenographic picture is different from that in children and may be confused with that of endothelioma.

5. The temperature and the blood cell counts are not so high as one might expect.

6. The lesion involves principally the marrow and the periosteum. There are spotty atrophy of the cortex and formation of light new periosteal bone if the lesion is in the shaft.

7. The lesion tends to be localized, without formation of sequestrums or involucrums.

8. Operation is indicated as soon as one suspects the presence of acute osteomyelitis.

9. Preceding infection elsewhere in the body is not usual.

10. There is usually no history of trauma.

11. The amount of pus present may be slight and may be encountered about the thickened periosteum before the shaft is opened.

12. Extensive saucerization is not usually indicated.

13. There is a tendency to involvement of the neighboring joint.

14. As with children, the involvement in adults is preponderantly among male patients.

15. The most important point in the diagnosis is the suspicion of the presence of the disease.

16. There seems to be no tendency to metastatic involvement.

FIBRIN STONES

REPORT OF FOUR CASES

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Renal calculi have been studied and their cause sought by a host of interested workers during the past several years. The brilliant investigations of Dr. Randall and his co-workers¹ have clearly pointed out the morbid processes in the formation of one type of renal stone. That there are other pathologic processes capable of producing renal calculi is plainly evident since the resulting bodies in the renal pelvis vary in composition and physical properties. The following 4 cases are submitted because the calculi were strikingly similar and appeared to present serial installments of identical pathologic processes. It is admitted that 4 cases are too few to justify dogmatic conclusions, yet only by the reporting of all cases of this kind will material be made available for further study.

REPORT OF CASES

CASE 1.—M. J. Z., a white man aged 43, had his first attack of pyelitis in 1934 and passed bloody urine on two occasions thereafter without urinary disturbance. The general physical examination, the blood count and the Wassermann test gave essentially normal indications. Two urinalyses showed no abnormality, and a third showed 15 white blood cells per high power field and a trace of albumin. The prostate was moderately enlarged, soft and boggy; the vesicles were palpable, and the prostatic smear showed from 13 to 25 white blood cells per oil immersion film. Cystoscopy revealed granular chronic posterior urethritis with polyp of the verumontanum and a moderate median bar. The mucosa of the bladder was normal. No obstruction was noted in either ureter. The capacity of the pelvis of the right kidney was 20 cc.; urine from this kidney showed 5 white and 10 red blood cells per high power field and a faint trace of albumin, and the stained smear of the urinary sediment showed no bacteria. The capacity of the pelvis of the left kidney was 30 cc.; urine from this kidney showed 5 white and 3 red blood cells and a faint trace of albumin, and the stained smear of the urinary sediment showed no bacteria. The plain roentgenogram of the kidney, ureter and bladder showed both kidneys in normal position and no opaque shadows suggestive of stones. Pyelograms revealed rather large pelvises with

1. Randall, A., and Melvin, P. D.: Morphogeny of Renal Calculus, *J. Urol.* **37**:737-745 (June) 1937. Randall, A.; Eiman, J. E., and Leberman, P. R.: Studies on Pathology of Renal Papilla: Relationship to Renal Calculus, *J. A. M. A.* **109**:1698-1702 (Nov. 20) 1937.

normal minor calices. Neither pelvis emptied normally. The patient was treated by prostatic massage and urethral irrigations. The polyp was fulgurated and the bar resected. The patient's condition improved markedly.

He was readmitted to the hospital on July 3, 1935, because of gross hematuria. Physical examination showed no abnormality. Cystoscopic findings were as follows: The neck of the bladder was healed; no bar was present; the right ureteral opening was swollen; bloody urine was escaping, and there was no obstruction in the ureter. The capacity of the right pelvis was 30 cc. The plain roentgenogram of the kidney, ureter and bladder with a catheter in the right ureter showed three faintly opaque masses of irregular shape lying near the tip of the catheter. The pyelogram revealed the right pelvis to be slightly larger than average with normal minor calices. The ureteropelvic junction was dilated to about twice the normal size. Occupying the interior of the pelvis was an irregularly shaped negative filling defect, but the filling defect itself was much larger than the faintly opaque shadows. This pyelogram was checked twice with identical findings (fig. 1 A). On July 10 the right kidney was explored for papilloma of the right pelvis. The pelvis, on being opened, was found to be filled with what was assumed to be a new growth, and a nephrectomy was therefore performed on the right. The patient's convalescence was uneventful, and there was no recurrence of the hematuria. The patient was seen within three months of the writing of this report and was in good health.

The pathologist's report follows:

"Microscopic Description.—The kidney had been incised when received at this laboratory. A mass measuring 3.1 by 1.3 by 0.8 cm. in its greatest thickness was present in the pelvis. The mass was dull gray and soft on palpation and cutting. A second mass, similar to the first, measured 1.2 by 1.1 by 0.7 cm. This mass showed moderate calcification. The pelvis of the kidney showed some infiltration by adipose tissue. The mucosa of the renal pelvis, especially its lower half, showed considerable congestion. The renal parenchyma showed no gross pathologic changes.

"Macroscopic Description.—In the glomeruli no pathologic change was demonstrable. A number of the tubules contained a pink-staining material suggesting casts. Sections of the mass in the renal pelvis showed no definite cellular structure or nuclei. The material took a light pink stain. Several deep-staining small areas had the appearance of an early stage of calcification.

"Diagnosis.—There was noncellular débris in the renal pelvis, some of it beginning to calcify. The renal pelvic area showed some infiltration with fat. Inflammation of the renal pelvis was present. The condition was not malignant." (Fig. 1 B).

A reexamination was reported as follows:

"Microscopic Description.—The mass in the renal pelvis consisted of unorganized débris. The structure appeared to contain occasional blood cells showing marked degenerative changes. No tumorous tissue was recognized. In the area of the pelvis of the kidney some adipose tissue was shown; there was a large number of leukocytes, plasma cells and fibroblasts; fibrous tissue and edema were present.

"Diagnosis.—Papilloma of the renal pelvis was not observed. The material had the appearance of markedly degenerated débris and blood cells. The renal pelvis was infiltrated with adipose tissue, and chronic inflammatory changes and fibrosis were present in this area."

CASE 2.—F. R. R., a white man aged 43, was admitted on March 11, 1936, because of tenderness in the right costovertebral angle, fever and pyuria. Three months previously he had had pneumonia. During convalescence marked tenderness in the left costovertebral angle and pyuria had developed. Urologic investigation had disclosed a rather large stone in the left renal pelvis and pyelonephritis on the left. The right kidney had been found normal. The stone, too large to be passed, had been removed by pelviolithotomy. The convalescence had been stormy, complicated by an acute attack of pyelonephritis on the right which necessitated catheterization of the right ureter and irrigation of the pelvis. Twenty-four hours prior to the current admission chills, fever and marked soreness of the right kidney had developed.

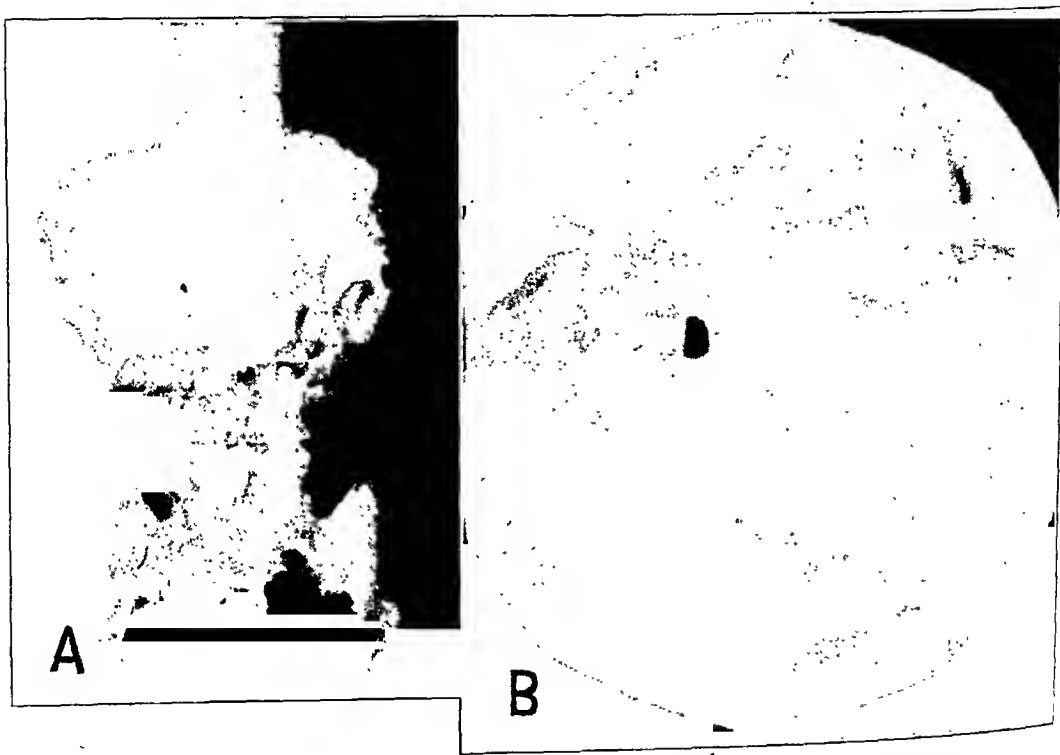


Fig. 1 (case 1).—*A*, right pyelogram showing a mass filling the right pelvis. *B*, high power photomicrograph of the mass of fibrin removed from the right pelvis.

The general physical examination showed no abnormality except for soreness of the right kidney, fever and pyuria. Cystoscopy revealed marked inflammation of the neck of the bladder and of the mucosa. The urine in the bladder contained free pus. The capacity of each renal pelvis was 18 cc. Urine from the right kidney contained 100 plus white and 8 red blood cells and gave a 4 plus reaction for albumin. The stained smear revealed a gram-positive coccus, which proved to be a short chain streptococcus. Urine from the left kidney contained 50 plus white and 8 red blood cells and a trace of albumin, and the stained smear revealed a gram-negative bacillus. On culture this organism proved to be *Bacillus coli*. The plain roentgenogram of the kidney, ureter and bladder showed both renal shadows to be in their normal position. In the region of the right pelvis there was a faint oval shadow $1\frac{1}{2}$ by $\frac{7}{8}$ inch (3.8 by 2.2 cm.). This mass

appeared to be laminated. The pyelogram showed the right pelvis to be larger than normal; the minor calices were slightly blunted and dilated, with the ureter joining the pelvis at its lowest point. There was a distinct impression of thickening of the pelvic and ureteral walls. The faintly opaque oval shadow appeared as a negative filling defect in the pyelogram and was seen to occupy the renal pelvis (fig. 2*A*). There was marked pelvic stasis. The left renal pelvis was larger than normal. Many of the minor calices were dilated and blunted. The ureter was not abnormal. Marked pelvic stasis was present. Analysis of the blood showed 34 mg. of nonprotein nitrogen, 15 mg. of calcium and 5.5 mg. of phosphorus per hundred cubic centimeters. There was 30 per cent excretion of phenolsulfonphthalein during the first hour and 10 per cent during the second

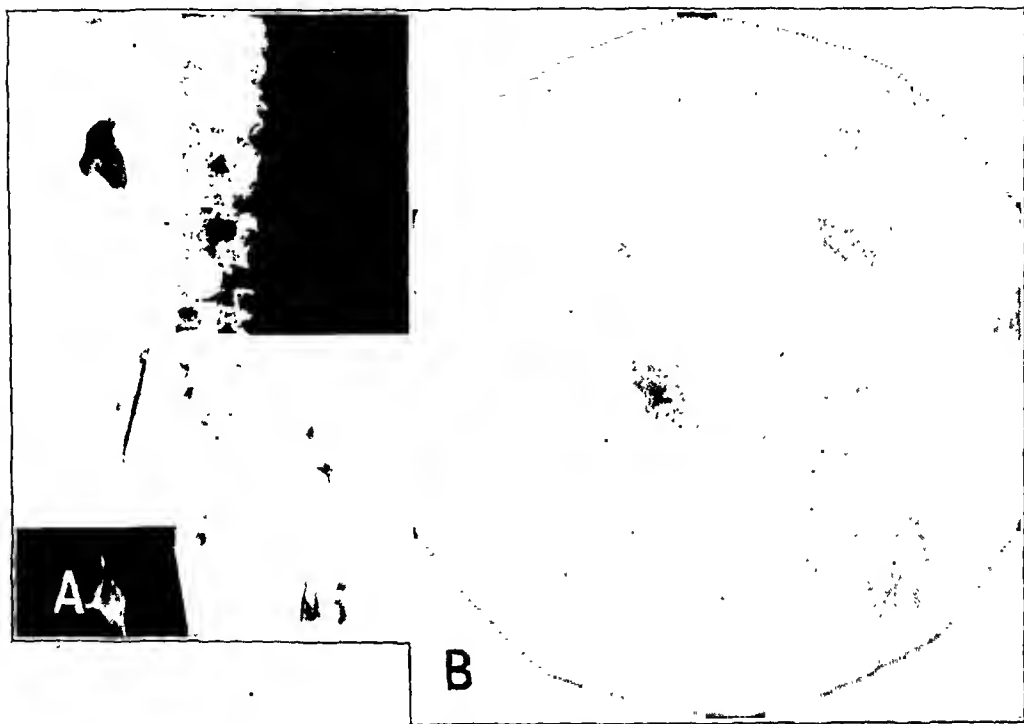


Fig. 2 (case 2).—*A*, right pyelogram showing a mass in the right pelvis. *B*, high power photomicrograph of the mass removed from the right pelvis.

hour after administration. The infecting organisms did not have the power to split urea. The basal metabolic rate was +3 per cent. Pelviolithotomy on the right was performed on July 28. The urine was still infected at the time of discharge despite all efforts at eradication of the infection. The stone or mass removed from the right pelvis was soft and putty-like with rounded margins; no calcification could be identified by inspection and palpation.

The pathologist reported as follows:

“Macroscopic Description.—The specimen consisted of a mass of material removed from the right renal pelvis and measured 3.7 by 3.2 by 1.2 cm. It was yellowish white with small blood-tinged areas on the surface and had the consistency and appearance of a piece of putty. On being cut into sections, the

specimen showed lamination; the center was yellowish white, the next layer light brownish yellow and the outer part yellowish white.

"Microscopic Description.—Considerable fibrin and degenerated debris were present. No other cellular elements were shown. Beginning calculous islands were shown in many areas.

"Diagnosis.—The material from the right renal pelvis contained no malignant tissue and showed no evidence of tuberculosis" (fig. 2 B).

CASE 3.—J. A. W., a white man aged 46, had his first attack of bilateral pyelonephritis in 1927. In spite of constant treatment by competent urologists this condition had progressed. In 1935 a stone was removed from the lower portion of the right ureter, and in 1936 a large calculus was removed from the bladder. He had remained well after a cystolithotomy until the early spring of 1937, when he began to suffer from chills, fever, pain, soreness in the left kidney and marked pyuria. On admission, on June 10, 1937, his temperature was 102 F., and his pulse rate 108. The leukocyte count was 14,000, with 83 per cent polymorphonuclears, the hemoglobin 50 per cent, the erythrocyte count 2,820,000 and the nonprotein nitrogen content of the blood 34.9 mg. per hundred cubic centimeters. Analysis of the urine showed alkaline reaction, albumin (4 plus) and 100 plus white and 15 red blood cells per high power field. Marked tenderness was present in the left costovertebral angle, and the left kidney was sore when palpated. Cystourethroscopy revealed marked cystitis with pus escaping from the left ureteral opening. On introduction of a catheter into the left renal pelvis, a large quantity of thick, foul-smelling pus escaped. Drainage of the left renal pelvis by catheter was instituted; two blood transfusions were given, and fluids were forced intravenously. Under this regime there was symptomatic improvement. Roentgen studies revealed the right renal shadow to be small. In the region of the left renal pelvis was seen an indefinitely shaped mass of faint density. The retrograde left pyelogram showed the opaque mediums distributed throughout the renal pelvis in an irregular manner. The left renal pelvis was evidently large and filled with some sort of material (fig. 3 A). After 20 cc. of diodrast was given intravenously, roentgenograms of the kidney, ureter and bladder made at ten, twenty, thirty and forty minute intervals, showed a small, atrophic right kidney with a small renal pelvis. The shadow of the left kidney was large, and the diodrast was excreted poorly by this kidney. There was a faint outline of the right renal pelvis in the thirty minute film and none of the left renal pelvis in the forty minute film. A recheck of the nonprotein nitrogen content showed it to be within normal limits.

On June 21, 1937, with the patient under spinal anesthesia, the left kidney was exposed. The left renal capsule was greatly thickened; the perirenal fat was chronically inflamed and indurated, and the lower two thirds of the kidney were filled with one large abscess and many small ones. The pelvis was filled with putty-like material. At operation the kidney was decapsulated, the cortical abscess excised as completely as possible and the putty-like material removed from the renal pelvis. The patient did not react from the operation and died at the end of twenty-four hours.

Following is a copy of the pathologic report on the specimens removed at operation:

"Macroscopic Description.—The specimen consisted of six pieces. One piece measured 3.2 by 2.1 by 1.2 cm. and had the gross appearance of hardened putty-like material. This piece cut readily, broke into debris and appeared somewhat gritty. The other five pieces of tissue were of similar appearance and ranged

from dirty white to yellow. These specimens had the gross appearance of adipose tissue and fat. The smallest of the five pieces measured 3.3 by 2.3 by 1.8 cm., and the largest measured 7.4 by 5.6 by 4.2 cm. Sections were taken from all pieces in various areas for microscopic study.

"Microscopic Description.—The specimen was made up of a large amount of adipose tissue and a large amount of tissue composed of lymphocytes, plasma cells and some eosinophils, the eosinophils and plasma cells often being arranged in clusters. An occasional blood vessel was shown" (fig. 3*B*).

"Diagnosis.—This case was one of soft renal stone (fibrin clot), with beginning phosphatic deposits; there were chronic inflammatory changes involving the renal cortex; no malignant growth or tuberculosis was present."

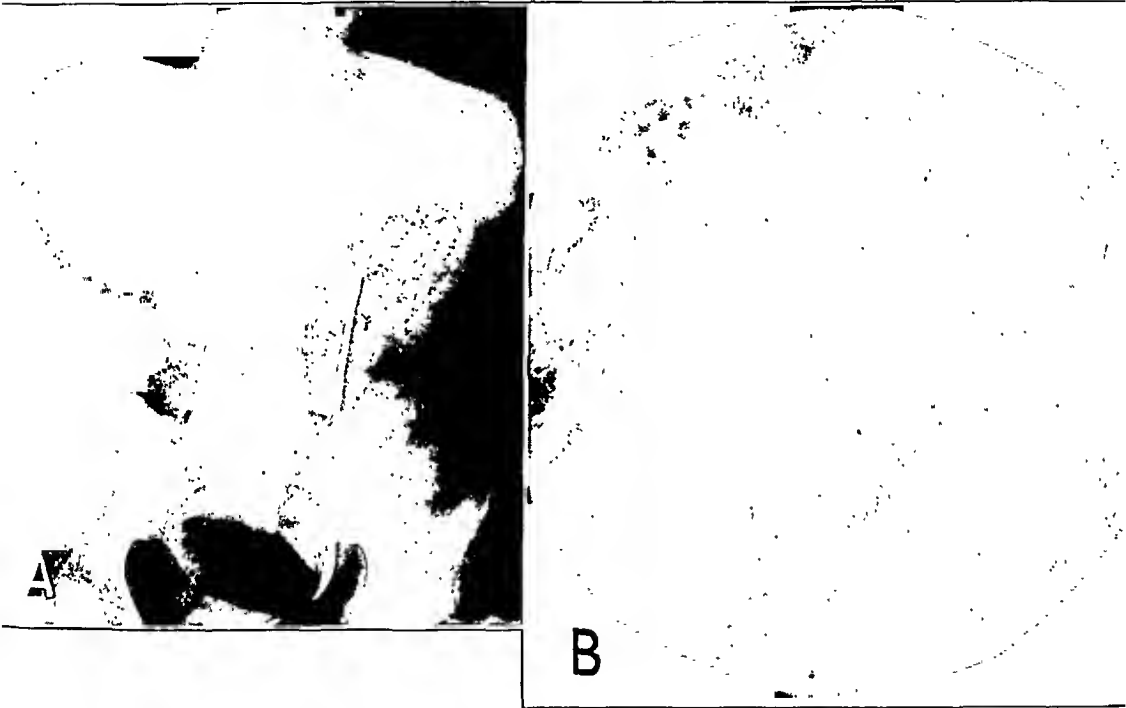


Fig. 3 (case 3).—*A*, left pyelogram showing the irregular distribution of opaque mediums through the pelvis. *B*, high power photomicrograph of the mass removed from the left renal pelvis.

CASE 4.—E. W. G., a white man aged 36, was admitted on Feb. 22, 1937, because of renal colic. The patient had a long history of renal colic on the right. pyelonephritis and calculus formation, culminating in nephrectomy on the right in the fall of 1936. The convalescence from nephrectomy had been uneventful, and the patient had been discharged from the hospital, only to return in February 1937, complaining of colic on the left side. At the time of admission his temperature was normal. Analysis of the urine showed an acid reaction, albumin (3 plus) and 100 plus white and 20 red blood cells per high power field. The blood count was within normal limits; the phenolsulfonphthalein test showed 32 per cent excretion in the first hour and 15 per cent in the second hour, making a total of forty-seven per cent. An intravenous pyelogram showed normal excretion of

diodrast. The pelvis was rather large; the minor calices were well cupped, and there were no abnormalities in the ureter. Opaque shadows suggestive of calculi in the kidney, the ureter or the bladder could not be made out. Shortly after admission the patient passed two small, soft and putty-like calculi. Cultures of material from these stones showed no urea-splitting organisms. The organism identified was *B. coli*, but the particular type was not determined. Analysis of these stones showed them to consist mainly of fibrin and myriads of coliform organisms. Efforts to eradicate the infection were unsuccessful, and when last seen, in July 1937, the patient was still passing calculi of a similar structure.

COMMENT

These calculi belong to a group classified as fibrin stones. Young² and Cabot,³ in their separate books on urology, each devoted one short paragraph to this type of stone. The literature has been incompletely searched, but so far nothing of interest has been found. The common pathologic process in the 4 cases reported was inflammation of the pelvic mucosa, but no one organism was present in all. The bacteria were not identified in the first case; in the second, a gram-positive coccus, which proved to be a short chain streptococcus, was found; in the third, *B. coli* and *Staphylococcus aureus* were identified, and in the last, *B. coli* appeared. None of these bacteria could split urea.

The calculi were similar in all the cases, appearing as soft, putty-like slightly yellow masses, which looked faintly opaque under roentgen rays only when large and appeared as filling defects in the retrograde pyelograms. Sections studied under the microscope showed fibrin and unorganized debris, with total absence of any cellular structure. In 3 cases areas of beginning calcification were seen. In all cases pelvic lavage with silver nitrate had been employed, but although silver is precipitated as insoluble chloride, chemical analysis of these masses did not show any silver. In case 4 the collections of fibrin were so small that the patient was able to pass them, and when he was last seen none had collected in the renal pelvis.

Speculating as to the mode of formation of these masses of fibrin, one is intrigued by the idea of an exudative inflammation of the renal pelvis. Those pelvises examined have shown an acute, diffuse, intense redness of the mucosa. Sometimes petechial hemorrhages have been present. The mucosa seems thickened and gives the impression of being edematous. Pelvic stasis was present in each case. With such a condition of the pelvic mucosa, it would seem reasonable to postulate the escape of fairly large quantities of serum into the pelvis with subsequent hardening similar to the crusting seen on cutaneous surfaces.

2. Young, H. H., and Davis, D. M.: *Young's Practice of Urology*, Philadelphia, W. B. Saunders Company, 1926, vol. 1, p. 374.

3. Cabot, H.: *Modern Urology*, ed. 3, Philadelphia, Lea & Febiger, 1936, vol. 2, p. 605.

Once a crust has been formed, the deposit of urinary salts, such as the triple phosphates of calcium, would of course occur with varying degrees of rapidity.

According to Berke,⁴ all stones have a matrix of more or less fibrin. The stones he examined all had varying degrees of hardness, but the material in the renal pelvis in our cases was soft, putty-like or rubbery and did not crush into fragments but was plastic to a certain extent, like dough. The sections were cut after the specimen was embedded in paraffin without decalcification. Although careful examination was made, no clumps of red blood cells could be identified, but an occasional ghost cell could be made out. The strands of fibrin predominated. It cannot be doubted that had these masses remained in the pelvis a sufficient length of time there would have been deposited in them sufficient amounts of the urinary salts to render them hard or at least harder than they were at the time of their removal. Another feature worthy of note in cases 1 and 2 is the large size of the masses and the rapidity of their development. In both cases pyelograms short periods before operation had shown no abnormality. In case 1 only was gross hematuria one of the symptoms, yet even in this case the mass failed to show clumps of red blood cells on section.

SUMMARY

1. Four cases of fibrin stones have been presented.
2. A theory as to their formation has been submitted.
3. In each case there seemed to be a different stage of the disease or at least a different symptomatic picture of the same basic pathologic process.

4. Berke, J. D.: Nature of Urinary Calculi, *J. Urol.* **38**:118-130 (July) 1937.

MALIGNANT ENDOMETRIOSIS OF THE OVARY, RESEMBLING ARRHENOBLASTOMA

REPORT OF A CASE IN A GIRL AGED NINETEEN

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A few years ago Meyer¹ classified certain ovarian tumors according to their biologic effects. The tumors were the arrhenoblastoma, which produces masculine changes, the granulosa cell, or feminizing, tumor and the dysgerminoma, which occurs in women with pseudohermaphroditism or poorly developed gonads. Both masculine and feminine features occurred in the case of ovarian cyst to be reported, but their relation to the cyst is perhaps questionable.

REPORT OF CASE

The patient was an Italian girl aged 19. She came to the hospital complaining of a third attack of sharp, continuous abdominal pain of twenty-four hours' duration, which had come at the end of a menstrual period; the others had preceded the last two menstrual periods and had been less severe. During the past year menstruation had occurred every three weeks, whereas it had taken place every four weeks previously since the age of 14. The change in menstrual frequency was accompanied by the development of a small mass in the lower part of the abdomen. According to the patient, the mass did not enlarge and had given no discomfort until the last two months.

Examination showed the patient to be slender and of moderate height. A masculine distribution of hair on the body was observed. A fairly thick mustache on the upper lip and a small beard on the chin had been present for three years. The voice was husky. The breasts were small, and the clitoris was not enlarged. Palpation revealed rigidity of the abdomen over a firm globular mass the size of a child's head in the midline. Secondary anemia was present and the leukocyte count was 15,000. The next day a large cyst of the right ovary was removed from its attachments to the pelvic wall and to the surrounding structures with difficulty. It was under great tension, and some of the contents escaped into the abdomen. The patient recovered and left the hospital in nine days. For four months she worked as a waitress, disregarding the advice that roentgen treatments were necessary, since a return of the symptoms might be expected. At the end of this time she was seized with sharp abdominal pain, which subsided when she rested in bed. Two weeks later she entered the hospital, as the abdomen had enlarged and there was a sensation of stretching of the skin. Examination showed the swelling to be symmetric; the percussion note was dull. The previous physical findings

From the Richmond Memorial Hospital.

1. Meyer, R.: Beitrag zur Frage der Funktion von Tumoren der Ovarien, Zentralbl. f. Gynäk. 54:2374, 1930.

were unchanged. The menstrual periods had continued to occur every three weeks. The hemoglobin content of the blood was 45 per cent; the leukocyte count, 13,000. A blood transfusion was given and the abdomen was opened. About 2 liters of reddish, viscid fluid containing numerous small, fairly firm, reddish slimy masses was removed. No growth was attached to any of the abdominal organs, nor was metastasis observed. The patient was comfortable for three weeks; then the abdomen again became enlarged. She was transferred for roentgen therapy and died shortly after admission. Permission for autopsy was not granted.

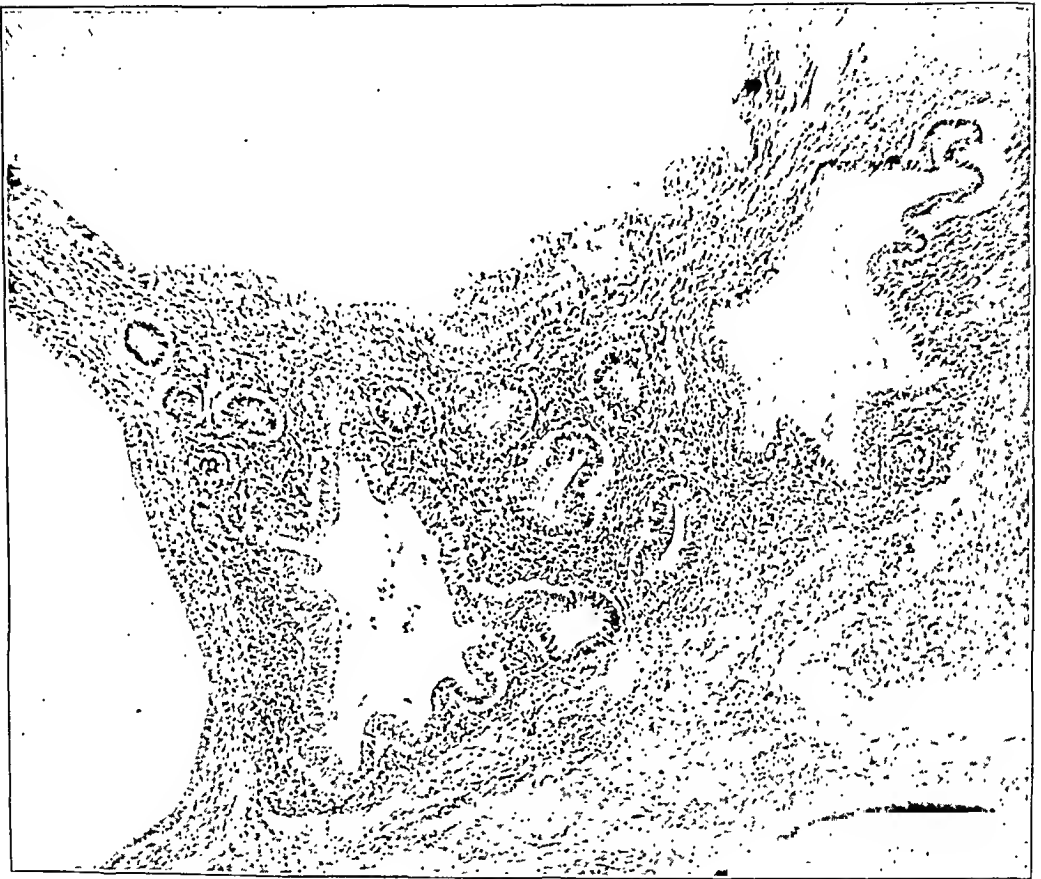


Fig. 1.—Endometrial glands and stroma in the cyst wall. Some blood cells are present in the lumen of the glands and cysts.

Gross examination of the cyst showed it to be open and 15 cm. in diameter. It was divided into two parts by thin fibrous tissue. The wall varied from 0.3 to 2 cm. in thickness. The thicker part was firm and white, with scattered reddish and yellow spots. In one place were a number of small, closely connected clear or brownish cysts. The lining of the cyst wall was for the most part thin and pale, but in the region in which the wall tapered downward both wall and lining were of soft hemorrhagic tissue. The contents of the cyst, except for several firm white masses, were thick coagulated blood and clumps of soft, rather gelatinous yellowish red tissue, attached in places to the cyst wall.

Microscopically, the outer covering of the cyst was composed of a few layers of fibrous tissue with a remnant of ovarian stroma and follicles on the external surface. The small area of cysts seen grossly was composed of glandular and cystic formations of various sizes, surrounded by thick stroma of fairly regular oval and spindle cells but divided by thin fibrous tissue showing numerous hemorrhages. High columnar epithelium with pink-staining cytoplasm formed the lining of the glands and the cyst. The lumens frequently contained red blood

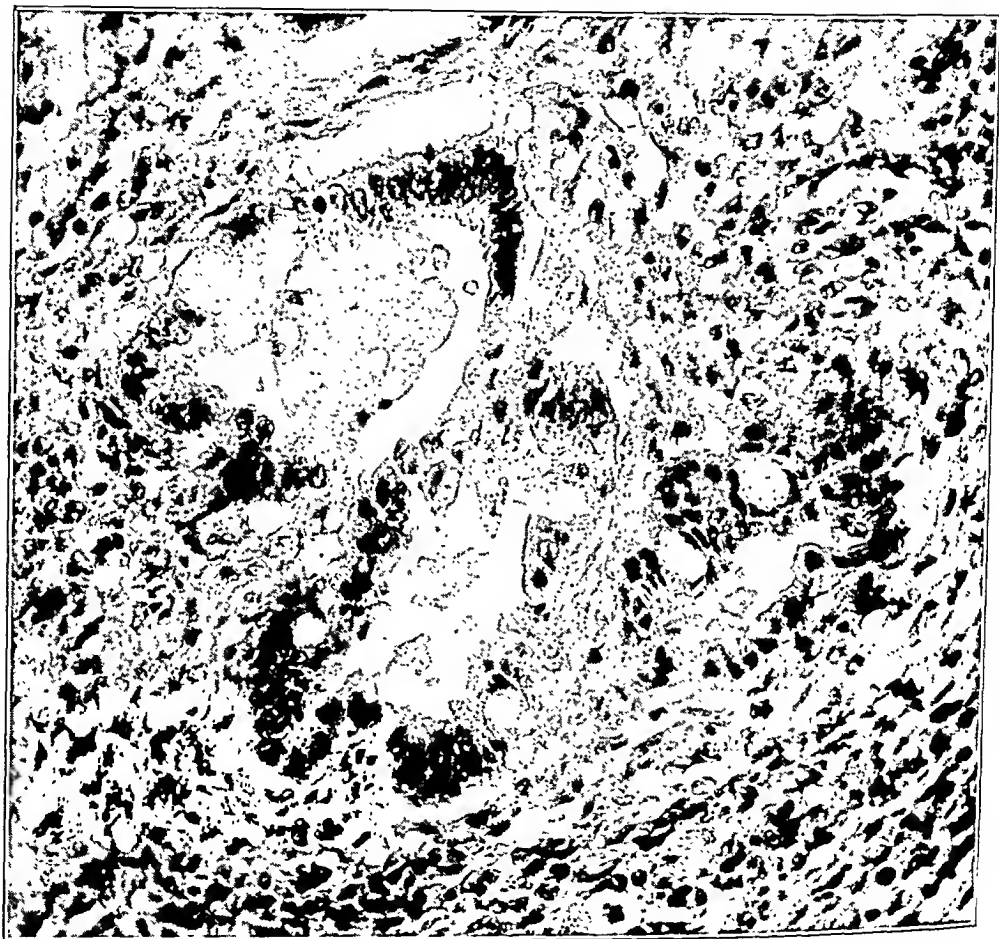


Fig. 2.—Early malignant change in the glandular cells of the endometrial area, with apparently nonmalignant stroma. The cells in one gland are tending toward a solid formation.

cells. This growth was similar to the glands and stroma of the uterine mucosa (fig. 1). In places the lining was papillomatous or made up of small round cells with clear cytoplasm. On the edge of the endometrial area were other glands with dark irregular cells and nuclei (fig. 2), although the stroma was apparently unchanged. Solid groups of small round cells staining light red were also present on the border of this area. The few cells left in the lining of the large cyst were columnar epithelium, but they were less uniform than those in the endometrial glands. A subepithelial remnant of apparently endometrial stroma occurred in one place.

The rest of the lining had been destroyed by the growth of the cyst wall. This was composed of a thin stroma of irregular, pale or deeply staining oval and spindle cells in which were hemorrhagic deposits, occluded vessels and various cellular formations. Many of the latter were closely packed glands or tubules, in which the cells had dark polymorphic nuclei and fatty cytoplasm (central group, fig. 3). The cytoplasm of the cells in other tubular islands was hyperchromatic, and the tubules frequently contained red blood cells. Some groups were mixtures of poorly formed glands and solid sheets of irregular, moderately large

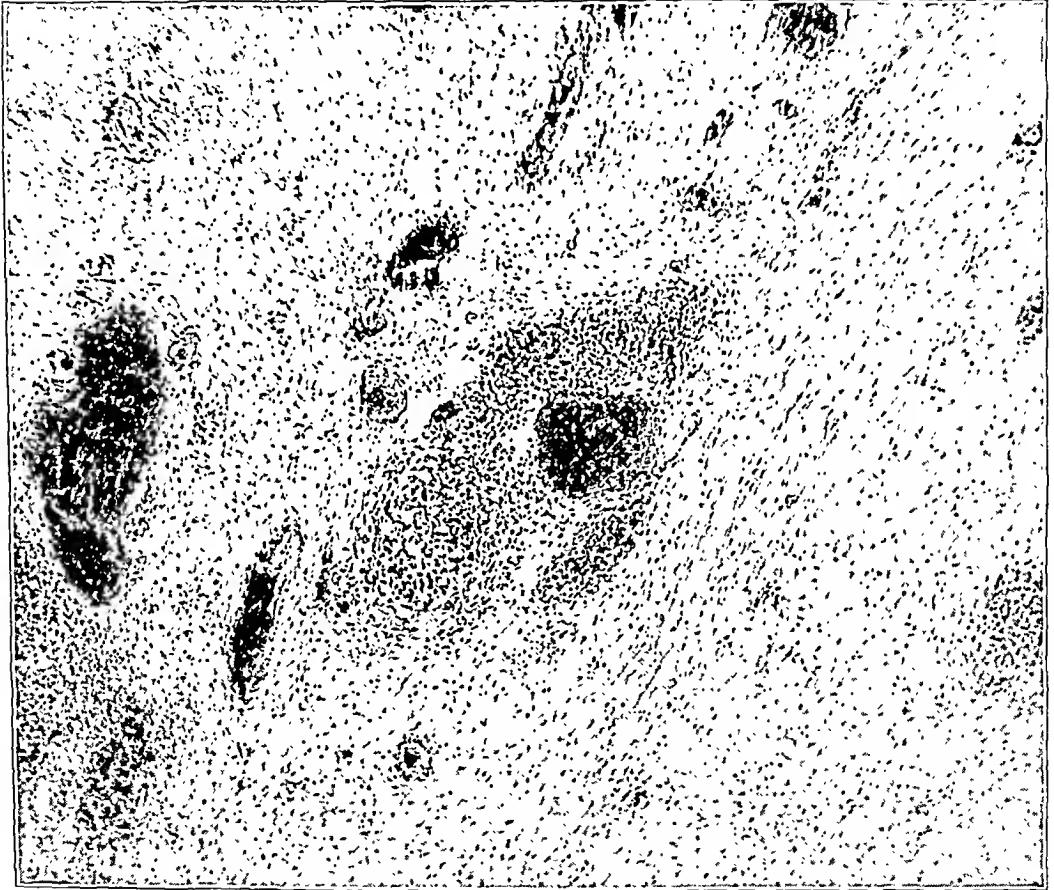


Fig. 3.—Cyst wall. In the stroma of irregular cells are congested vessels, hemorrhages and resultant fatty necrosis of the cells in the island of tubular carcinoma.

reddish cells. Other groups contained only hyperchromatic spindle cells in thick, formless union. They also occurred as thin bundles between glands and partially formed glands of cells with dark oval nuclei and scanty cytoplasm, as in part of a group shown in figure 4. These spindle cells among the diverse combinations and formations of the cellular islands were similar to the hyperchromatic cells in the stroma of the cyst wall. Heavy bundles of them projected into the lumen of the cyst but contained many hemorrhagic deposits and were partly necrotic. The second growth in the abdomen was formed of dense whorls of hyperchromatic,

irregular spindle cells in a thin stroma of similar cells. Its cells resembled both the intraluminal cells and the formations in the cyst wall. Glands or tubules (the terms have been used interchangeably) were not observed, although it is possible that they had been destroyed by necrosis and by hemorrhages. Figure 5 indicates the type of growth and of cells, many of which show mitosis while others show karyorrhexis.

COMMENT

Since the area of endometriosis was an integral part of the cyst wall, the entire cyst was identified as an endometrial cyst which had become malignant. This conclusion is upheld by the abnormal reproduction of the glands and stroma of the endometrial area in the cyst

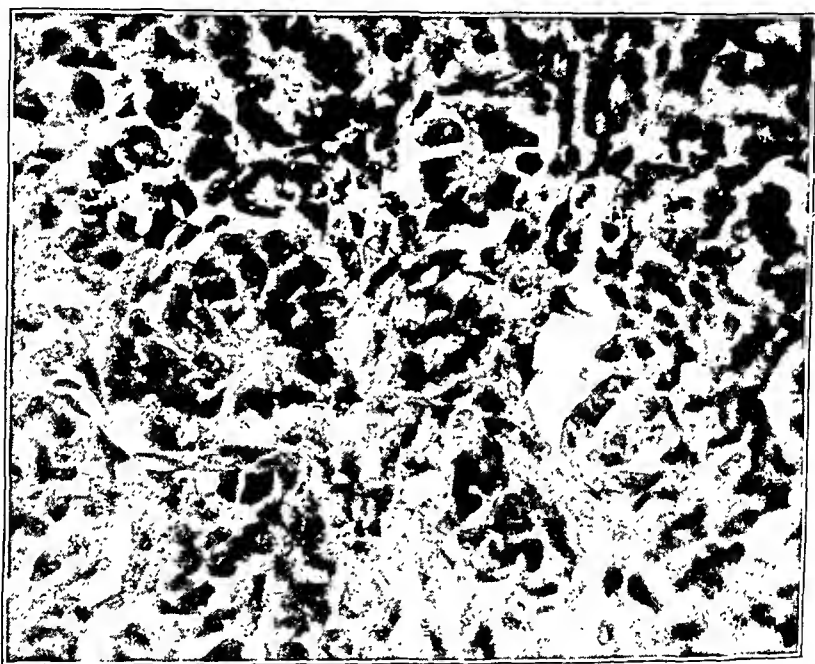


Fig. 4.—Carcinosarcomatous group in the cyst wall. The cells of the tubules are somewhat similar to the irregular ones in the glands, shown in figure 2.

wall. Moreover, the change in the shape and size of the cells and their nuclei in the outer glands of the endometrial area, as shown in figure 2, is proof of early malignancy linking this area with the malignant growth of the cyst wall. This is further substantiated by the irregular oval and spindle cells (fig. 4) which resembled the nonmalignant stroma cells (fig. 2) and were similar to the malignant cells (fig. 5).

The formation of the cyst wall was unusual. However, not only were the islands of tubular growth, faintly seen in figure 3, similar to uterine carcinoma, but the sarcomatous stroma around these tubules and the partly sarcomatous, partly carcinomatous growth (fig. 4) were even

more suggestive of carcinosarcoma of the uterine mucosa. This type of growth, although rare, according to Meyer,² may occur in extrauterine areas of endometriosis as well as in the uterus. It seems probable that

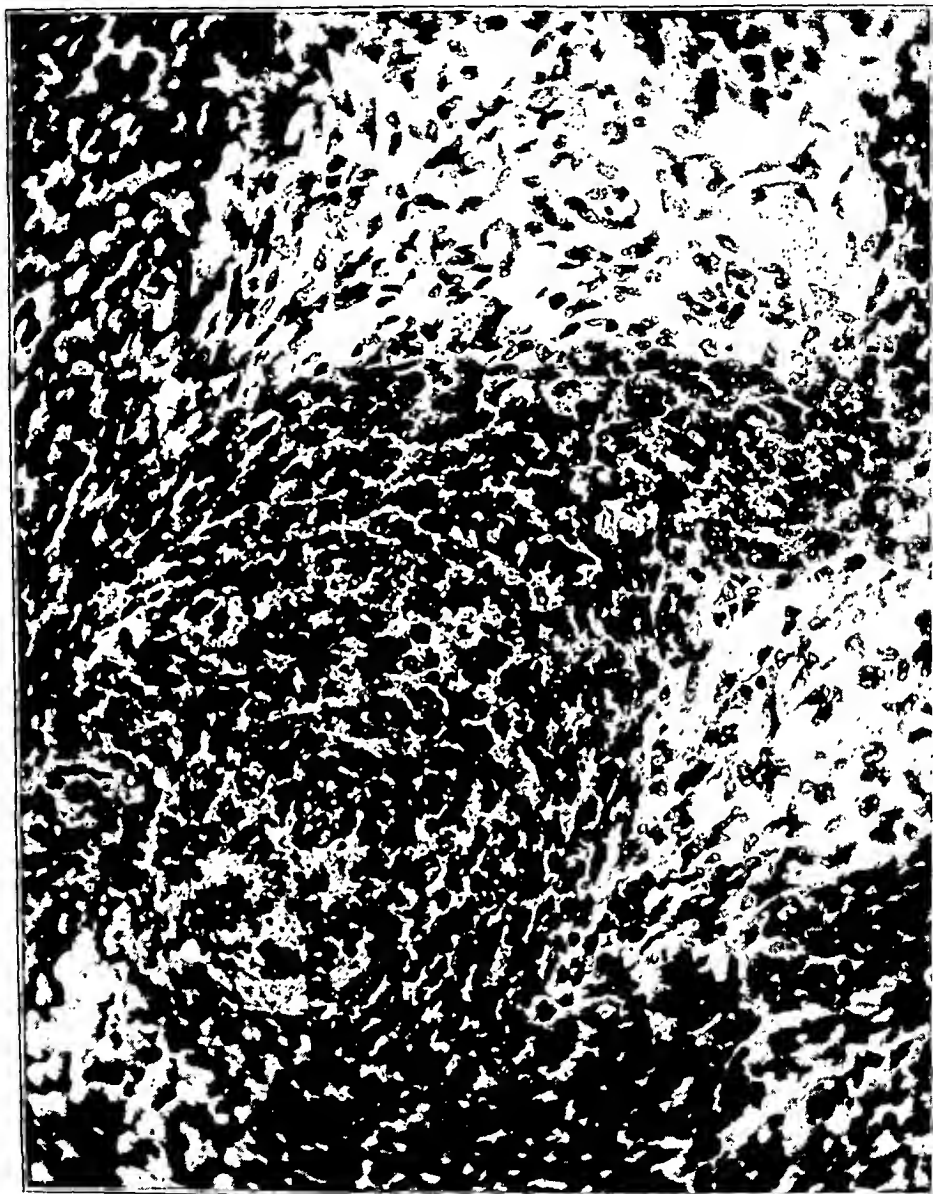


Fig. 5.—Recurrent abdominal growth of dense groups of hyperchromatic spindle cells in a thin stroma of the same cells. Karyorrhexis and mitosis are prominent. The cells are not unlike those of the stroma in figure 2 and more definitely resemble those seen in figures 3 and 4.

2. Meyer, R., in Henke, F., and Lubarsch, O.: *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1930, vol. 7.

it may be found in the ovary, although carcinoma has been the sole malignant tumor reported associated with ovarian endometriosis.³ The recurrent growth in the abdomen was similar to the group formations in spindle cell sarcoma of the uterine mucosa² and may be traced to the contents of the cyst.

However, sarcomatous and tubular growths are not confined to the uterine mucosa but are characteristic of ovarian arrhenoblastoma. Of the three types of tumor designated by this name, ranging from benign tubular adenoma to the type resembling sarcoma, the present cyst might be classified as of the intermediate type, which embraces the features of the first and the last. Yet arrhenoblastoma is not sarcoma but a tumor of undifferentiated cells that may or may not be malignant. As fatty and deep pink-staining round cells are also found and identified as interstitial cells, similar ones in the cyst wall might suggest arrhenoblastoma. The specificity of these cells to arrhenoblastoma, however, has been questioned by Novak and Gray.⁴ In the cyst herein described the sheets of pink-staining cells were evidently derived from the glands, and the fatty ones were the result of circulatory disturbance. Although the cyst and the succeeding growth were malignant formations of well differentiated cells, some support is given to the consideration of arrhenoblastoma by the masculine characteristics of the patient. One of these, hirsutism, in the opinion of Novak and Long⁵ and of Schiller,⁶ may be found in normal women. Schiller concluded also that its presence is not only variable in arrhenoblastoma but that it does not always disappear with the removal of the tumor and may be associated with all kinds of ovarian growths. As the mother and sister of the patient in this case also had fairly heavy mustaches and deep voices, the hirsutism and the virile voice of the patient were perhaps exaggerations of familial traits. The boyish figure in a family of obese members might be regarded as a biologic effect of the tumor, but the anemia must be considered, as must the occurrence of all these characteristics before the recognition of the tumor in the abdomen. If the growth were a masculinizing one, its recurrence should not have been attended by the unchanged continuity of any biologic effects but by their greater manifestation. Moreover, the only apparent influence of the tumor was the increase in frequency of menstruation to once every

3. Sampson, J. A.: Carcinoma of the Ovary, *Arch. Surg.* **10**:1 (Jan.) 1925.
Hauser, R.: Carcinom auf der Basis ausgedehnter Endometriose, *Ztschr. f. Krebsforsch.* **43**:306, 1936.

4. Novak, E., and Gray, L. A.: Clinical and Pathologic Differentiation of Certain Special Ovarian Tumors, *Am. J. Obst. & Gynec.* **31**:216, 1936.

5. Novak, E., and Long, J. H.: Ovarian Tumors Associated with Sexual Changes, *J. A. M. A.* **101**:1057 (Sept. 30) 1933.

6. Schiller, W.: Zur Frage der Spezifitaet vermaennlicher ovarial Tumor. *Arch. f. Gynäk.* **160**:344, 1935.

three weeks, since this was coincident with the appearance of the growth in the abdomen. Such a reaction, however, is symptomatic of granulosa cell tumor or of endometriosis rather than of arrhenoblastoma. In this case the menstrual increase was doubtless due to the endometrial character of the cyst.

SUMMARY

An ovarian cyst which occurred in an Italian girl aged 19 is considered a carcinosarcoma arising in an area of endometriosis. A spindle cell sarcoma of the type found in the uterine mucosa recurred in the abdomen four months after removal of the cyst. Masculine distribution of hair and a husky voice are considered exaggerated familial traits in the patient, since they were present to some extent in the mother and sister and since they antedated the recognition of the tumor in the abdomen. The growth was accompanied by an increase in frequency of menstruation during the year preceding its removal. Slenderness and small breasts are perhaps effects of debilitation by the tumor.

MYOBLASTIC SARCOMA OF THE URINARY BLADDER

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Sarcomas constitute only a small proportion of the malignant growths arising in the urinary bladder. Many varieties of sarcoma are mentioned in classified lists, but some names suggest vaguely the parent tissue origin or indicate merely a poorly differentiated variety of cell components. Only a few muscle tumors are included in these lists. Munwes¹ in 1910 recorded 5 myosarcomas as occurring among 94 sarcomas of the urinary bladder. Hückel's² review, published in 1934, mentioned the occurrence of 8 leiomyosarcomas and 3 rhabdomyosarcomas among 125 sarcomas of the urinary bladder.

The details of cell structure in many descriptions of sarcoma of the urinary bladder are meager, especially in descriptions of sarcomas of muscle tissue. The latter tumors are of two types, the smooth and the striated muscle tumors. When the cells of a rhabdomyosarcoma do not become differentiated beyond the myoblastic stage, characteristics other than the cross striations are necessary to permit the conclusion that the growth originated in skeletal muscle.

Abrikosoff³ divided myoblastic tumors into the following four types: (1) pure myoblastoma with cells devoid of striations; (2) a tumor composed of myoblasts similar to those in the first type of tumor, with longitudinal or cross striations, or both, often imperfectly developed; (3) a tumor composed of hypertrophied myoblasts, including some of great size, frequently multinucleated, syncytial, with or without striations; and (4) malignant myoblastosarcoma, or myoblastic sarcoma, a polymorphous cell tumor, structurally resembling the more differentiated

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1. Munwes, C.: Zur Statistik und Kasuistik der Blasensarkome, *Ztschr. f. Urol.* 4:837, 1910.

2. Hückel, R.: Sarcoma der Harnblase, in Henke, F., and Lubarsch, O.: *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1934, vol. 6, pt. 2, pp. 655-667.

3. Abrikosoff, A. I.: Ueber Myome ausgehend von der quergestreiften willkürlichen Muskulatur, *Virchows Arch. f. path. Anat.* 260:215, 1926; Weitere Untersuchungen über Myoblastenmyome, *ibid.* 280:723, 1931.

rhabdomyosarcoma. Cappell and Montgomery⁴ considered this grouping unsatisfactory, for they stated that all variations of cells may be found in a single tumor. They suggested that striated muscle tumors be classified into two types, those with cross striations and those without. Their first type includes (a) simple rhabdomyoma with well differentiated muscle fibers but no primitive or anaplastic forms and (b) malignant rhabdomyoma with some cells having distinct cross striations. Their second type includes growths the cells of which have the staining qualities of muscle and morphologically contain spindle-shaped and hypertrophied myoblasts. The cells are without striations or have delicate striations demonstrable by special stains. This form of tumor corresponds to the first type in Abrikossoff's classification. The muscle tumors reported so far, Cappell and Montgomery⁴ stated, have been benign except the tumor of the thigh described by Muller⁵ in 1917, which they considered malignant. Cappell and Montgomery concluded that the term myoblastoma should be restricted to skeletal muscle tumors the cells of which have no cross striations.

In Rakov's⁶ recent report on malignant tumors of skeletal muscle the descriptive term "malignant rhabdomyoblastoma" was used. The tumor cells, he stated, are polymorphic, although the predominant form is elongated and spindle shaped. Other tissue elements are polymorphous cells and giant cells. Longitudinal fibers in the elongated cells occasionally have cross striations; pronounced striations rarely are found.⁷

Sarcomas of smooth muscle, according to Geschickter⁸ and others, repeat the histogenesis of this tissue and consist of compactly arranged spindle-shaped cells. Geschickter⁸ stated that sarcomas of striated muscle may duplicate the structure of the spindle cell sarcomas of smooth muscle or may have the large elongated multinucleated cells of the myoblastic stage.

REPORT OF A CASE

A white man aged 72 entered the service of Dr. Harry Culver at St. Luke's Hospital on March 6, 1937, because of hematuria and "bladder gravel" for three months, associated with frequent voiding, nocturia and dysuria. Litholapaxy and transurethral resection of the prostate had been done three years previously,

4. Cappell, D. F., and Montgomery, G. L.: On Rhabdomyoma and Myoblastoma, *J. Path. & Bact.* **44**:517, 1937.

5. Muller, H. R.: Traumatic Rhabdomyosarcoma Following Successive Fractures of the Femur, *J. Cancer Research* **2**:393, 1917.

6. Rakov, A. I.: Malignant Rhabdomyoblastomas of Skeletal Musculature, *Am. J. Cancer* **30**:455, 1937.

7. Hirsch, E. F.: Malignant Rhabdomyoma of the Leg, *Arch. Path.* **8**:9 (July) 1929.

8. Geschickter, C. F.: Tumors of Muscle, *Am. J. Cancer* **22**:378, 1934.

and one year previously a nephrectomy had been done on the right side because of renal concretions and pyonephritis. Roentgenograms taken soon after the patient's admission demonstrated a diverticulum of the urinary bladder and osteoporosis of the pelvic bones; the latter was interpreted as due to metastases of a malignant tumor. He had a nephrectomy scar on the right side with hernia. Cystoscopic examination demonstrated an incrustated tumor of the urinary bladder, cystitis, obstruction of the neck of the bladder and stricture of the anterior portion of the urethra. Surgical suprapubic drainage of the bladder on March 23 gave some relief. The patient died on April 26, about four and a half months after the onset of hematuria, one year after the nephrectomy and three years after transurethral resection of the prostate.

Postmortem examination was restricted to the chest and abdomen. The essentials of the anatomic diagnosis were: extensive diffuse infiltrative myoblastic sarcoma of the urinary bladder; metastatic myoblastic sarcoma of the periaortic and abdominal lymph nodes, the lungs, the liver, the right adrenal gland and the bodies of the twelfth thoracic and first to fifth lumbar vertebrae; suppurative urinary cystitis; acute fibrinous pelvic peritonitis; constriction of the left ureter by myoblastic sarcoma; pyoureter, and suppurative pyelonephritis and perinephritic abscess on the left side. The urinary bladder, an indurated thick mass, extended 7.5 cm. above the symphysis pubis. Friable gray tissues bound the bladder to the parietal peritoneum anteriorly on the right side. Nodules of gray tumor tissue, 1 cm. in diameter, roughened the hyperemic posterior surface. Other nodules extended into the left groin. The entire lining of the urinary bladder was necrotic. Hemisected through the midsagittal plane, the wall (fig. 1) was seen to be firm in all portions, with friable gray tissues, ranging in thickness between 1 and 4 cm. The thinnest portion was in the trigon. Behind the protruding tissues between the ureteral openings was a recess. Only a small amount of prostate tissue remained. The diameter of the left ureter above the urinary bladder was 2.5 cm. Near the bladder the ureter was encased in tumor tissue. The ureteral orifice in the bladder was 2 mm. in diameter. The seminal vesicles and the vas deferentia had no noteworthy changes. The bodies of the twelfth thoracic and of all the lumbar vertebrae contained nodules of metastatic tumor tissue. The gross structure of the rami of the right os pubis and of the right ilium was unchanged. The amount of red marrow tissue in the ribs was small. Each lung had many nodules of metastatic tumor tissue, ranging from 1 to 15 mm. in diameter. They were distributed mainly in the subpleural tissues. There were also metastases in the liver varying from 3 to 10 mm. in diameter and a nodule in the right adrenal gland 1.5 cm. in diameter. The large left kidney contained many abscesses and a cortical retention cyst 6 cm. in diameter. There was also a large perinephritic abscess on the left side. The periaortic abdominal lymph nodes were enlarged by gray tumor tissue.

Sections of the primary and secondary tumors were stained with hematoxylin and eosin, phosphotungstic acid-hematoxylin, Mallory's aniline blue, Masson's trichrome stain, Van Gieson's stain, Heidenhain's iron-hematoxylin stain and Laidlaw's silver impregnation for reticulum. The edge of the lining of the urinary bladder was necrotic. All but small masses of the original smooth muscle in the wall consisted of tumor tissue. Fine collagenous fibers formed a delicate supporting mesh for large and small spindle-shaped cells, polymorphous cells and large multinucleated giant cells (fig. 2). There was no regularity of tissue structure, all varieties of tumor cells being combined in different proportions and density. They had the staining qualities of smooth muscle cells. The spindle-

shaped cells ranged in size from that of the usual smooth muscle cell to six or eight times this dimension. The cytoplasm of the small forms contained an elongated or vesicular nucleus with a few fine and coarse chromatin granules. The large spindle cells had proportionately more cytoplasm and larger nuclei; some had several nuclei. The polymorphous cells varied also in size and shape. They had an abundant cytoplasm, oval or lobed vesicular nuclei containing coarse and fine chromatin granules and a distinct cell membrane. Large cells with a sharp membrane and a single nucleus and multinucleated protoplasmic masses in bands were the least numerous cells. Among the tumor cells were many in

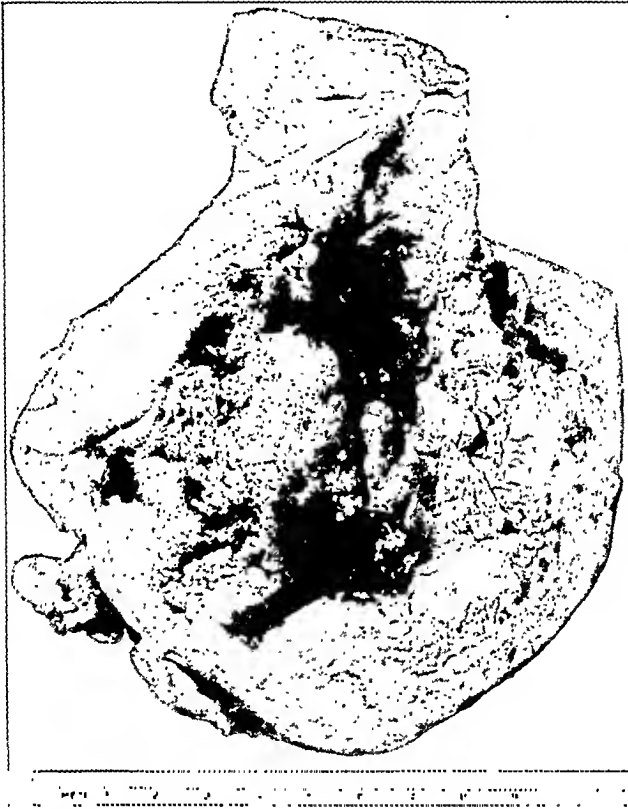


Fig. 1.—Photograph of the urinary bladder hemisected through the mid-sagittal plane. The prostatic urethra is shown at the left side of the photograph; the cystotomy fistula and the cutaneous tissues of the abdomen are shown above. The wall of the bladder in general is markedly thickened by the growth of sarcoma tissues.

mitosis, some in atypical form. The cellular tumor tissue extended through the wall of the urinary bladder into the subperitoneal tissues. Many dilated blood and lymph channels had thrombi of tumor tissue. The sections stained with Heidenhain's iron-hematoxylin, phosphotungstic acid-hematoxylin, Mallory's aniline blue and Masson's trichrome stain had sharply contrasted tissues. The collagenous fibers formed only a small portion; the myoblastic cells, a considerable portion. The cytoplasm of the large spindle-shaped cells and the protoplasmic masses had



Fig. 2.—Photomicrographs illustrating three main varieties of myoblastic cells in the sarcoma of the urinary bladder: *A*, large spindle cells; *B*, polymorphous cells, and *C* multinucleated protoplasmic cells.

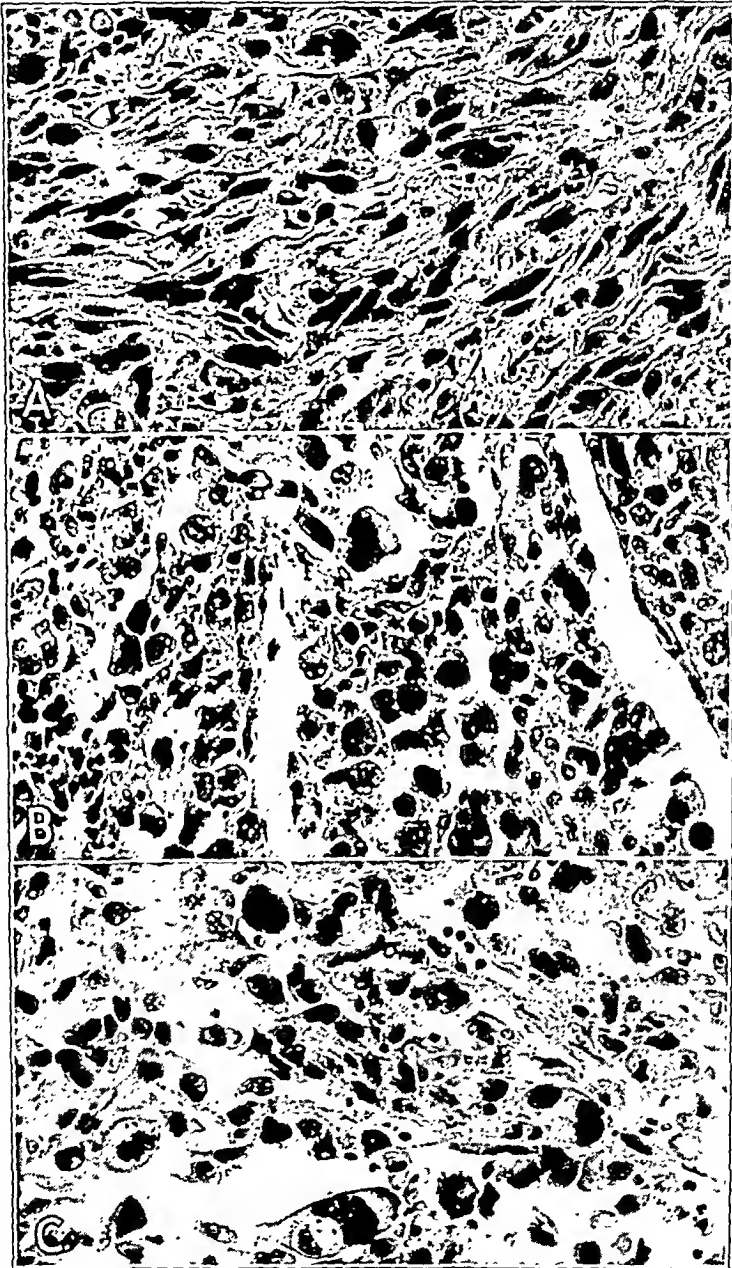


Fig. 3.—Photomicrographs illustrating the cellular structure of the metastases: *A*, spindle cells in a nodule of the liver; *B*, polymorphous and some multi-nucleated forms in a lymph node, and *C*, protoplasmic and other cells in the secondary growth of the right adrenal gland.

fine longitudinal fibrils, but a thorough search failed to disclose cells with cross striations or cells with concentrically arranged barred fibrils, as described by Wolbach.⁹

The metastases in the lungs, the liver, the right adrenal gland, the lymph nodes and the vertebrae (fig. 3) had similar cellular tissues composed of tumor cells in various proportions.

COMMENT

The histologic structure and the staining qualities of the tumor cells in this malignant growth of the urinary bladder indicate an origin in muscle. Myoblasts of various kinds, including spindle-shaped cells, polymorphous cells and hypertrophied forms, some of great size, were present. Fine longitudinal fibrils were demonstrated in some of the spindle cells and in the hypertrophied myoblasts. The search for cross striations in these cells was unsuccessful, although sections from many regions stained with Heidenhain's iron-hematoxylin and phosphotungstic acid hematoxylin were examined.

Leiomyosarcomas arising in the urinary bladder and other viscera, according to Geschickter⁸ and Krauskopf,¹⁰ contain spindle-shaped cells with vesicular, oval or elongated nuclei, but no polymorphous cells or large multinucleated protoplasmic masses. The presence of these large cell forms suggests the origin of the sarcoma in striated muscle tissues. Skeletal muscle tumors of the urinary bladder have been ascribed to displaced myotome tissues. Geschickter⁸ stated that the association of rhabdomyomas with smooth muscle in the genital tract may be due to metaplasia of voluntary muscle from smooth nonstriated forms. This origin is not generally accepted, and such a view is unnecessary because of the proximity of skeletal muscle tissues at the base of the urinary bladder.

MacKenzie and Chase¹¹ found a few published references to malignant skeletal muscle tumors of the urinary bladder. They described a malignant localized rhabdomyosarcoma of the trigon, occurring in a woman aged 69; there were metastases to the wall of the duodenum, to the liver and to the portal lymph nodes. The tumor tissues contained many spindle-shaped cells, undifferentiated cells and large multinucleated cells. The large cells suggested the myoblastic nature of the growth, but cross striations or fibrillations were not found in the cells of the tumor. A few cells with cross striations were demonstrated in the metastases of the liver and the duodenum after search in serial sections.

9. Wolbach, S. B.: A Malignant Rhabdomyoma of Skeletal Muscle, *Arch. Path.* 5:775 (May) 1928.

10. Krauskopf, H.: Report of an Unusual Case of Leiomyosarcoma Occurring in the Urinary Bladder, *Am. J. Obst. & Gynec.* 24:133, 1932.

11. MacKenzie, D. W., and Chase, W. H.: Rhabdomyosarcoma of the Urinary Bladder with Metastases, *J. Urol.* 19:315, 1928.

White¹² described briefly a pedunculated rhabdomyosarcoma excised from the urinary bladder of a child. Welfeld, Hill and Hillebrand¹³ found only 3 reports of malignant skeletal muscle tumors of the urinary bladder. These were the report by Houette of a congenital diverticulum in the bladder of a boy aged 13 months; the report of a rhabdomyosarcoma by MacKenzie and Chase, which has been mentioned; and the tumor described by Monserrat and Garcia as occurring in a man aged 43. Welfeld, Hill and Hillebrand described 2 polypoid malignant tumors of the skeletal muscle, occurring in children.

The evolution of the myoblastic sarcoma of the urinary bladder here described seems to follow the usual course of sarcomas. Large blood channels about the bladder were invaded extensively by tumor tissues. These thrombi of tumor tissue doubtless were important in the metastatic spread of the disease to the liver, to the lungs and elsewhere.

SUMMARY

Myoblastic sarcoma occurs rarely in the urinary bladder. The growth described in this report diffusely infiltrated the bladder of a man aged 72. There were metastases to the lungs, the liver, the right adrenal gland, the spine and many lymph nodes. The tumor cells had the staining qualities of muscle tissue. They consisted of spindle cells, polymorphous cells and large multinucleated protoplasmic cells. Some of the large tumor cells had longitudinal fibers. Cells with cross striations were not found.

12. White, H. P. W.: Tumor Removed from a Child's Bladder, *Proc. Roy. Soc. Med.* **22**:1382, 1929.

13. Welfeld, J.; Hill, L., and Hillebrand, J. G.: Rhabdomyosarcoma of the Urinary Bladder, *J. Urol.* **36**:150, 1936.

DEAD (OX) FASCIA GRAFTS IN TENDON DEFECTS

AN EXPERIMENTAL STUDY

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Considerable difference of opinion exists regarding the healing of tendons and tendon grafts. The principle of Roux states that the end result of a transplant in which biologic laws have been observed depends largely on whether or not the functional activity for which the tissue was originally intended has been assumed early. The tension to which the graft should be subjected is also a perplexing problem. The postoperative treatment of tendon grafts differs from that of grafts in other parts of the body, for example, in skin and in bone. With the latter, immobilization is essential in establishing a vascular supply; with the former, immobilization tends to form adhesions which defeat the purpose of the graft.

HISTORICAL DATA

Until the middle of the eighteenth century, surgeons were largely influenced by the opinions of Galen, who taught that tendons are a mixture of nerves and ligaments the suturing of which is followed by twitchings of pain and by convulsions. It was not until after 1750, when Haller demonstrated the insensibility of tendons, that operative procedure on them was generally resorted to. Hunter in 1767 was the first to study the processes of tendon repair experimentally in dogs. He concluded that tendons heal by means of callus produced in a manner similar to that by which bone callus is produced.

Later experimental work led to a number of different theories of tendon repair. According to some of these, a formless exudate is first produced; then the tendon stumps generate new tendon. The tendon sheath was considered by others to be the sole factor in repair. According to another theory, cells from the blood, wandering into the defect, are responsible for the healing process. By another school of thought, the connective tissue surrounding the stumps was believed to be the most important element in healing.

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Roux (1780-1854) was among the first to stress the importance of function in the formation of tendon or tendon-like tissue. This led to extensive study of grafts in tendon defects. Kirschner in 1909 published the results of an experimental study of autoplasmic tendon and fascial grafts. He found that fascia took on the character of tendon. Rehn in 1910 studied the effect of transplantations of all sorts of tissues grafted into tendon defects or into other areas in which they were not subjected to function. He found that nonspecific tissues when grafted into tendon defects and subjected to stress and strain took on a tendon-like character.

The first experimental work with fascia in the United States was done by J. Staige Davis. He had been working for some time before he discovered that Kirschner had just published some work along the same line. Davis stated that after looking for suitable tissue which was easily obtainable and which had considerable strength and sufficient flexibility he was led to try the experimental transplantation of free flaps of fascia. He performed 62 experiments on 39 dogs. Most of the flaps were from the iliotibial bands, and when adhesions were not desired the transplant was placed with the inner, or muscle, surface exposed. He successfully transplanted free fascia to the subcutaneous tissue, to muscle, to periosteum, to naked bone, to cartilage, to tendons and to ligaments. He showed that defects in muscle and tendon could be bridged by free flaps of fascia. He successfully transplanted free flaps of fascia around arteries, veins and nerves without interfering with the lumen of the vessels or compressing the nerves. He inserted free flaps of fascia in joints, substituted flaps of fascia for the patella and sutured bone fragments together.

He prepared defects in the skull and substituted free flaps of fascia; this procedure resulted in the formation of a strong membrane between the dura and the edges of the bone. In other experiments he removed the dura as well as the bone, and the fascia united firmly to the cut edges of the dura. The flap also seemed to serve equally well for the repair of tracheal defects. He successfully placed transplants in defects in the abdominal wall, suturing flaps of fascia into peritoneal and muscle fascia defects. He was also able to cure experimentally produced hernias. He tried such grafts in the stomach, the intestines, the bladder, the liver, the kidney and the spleen, with apparent success. In most of his experiments the transplant was immediately grafted into the same animal from which it had been taken. He, however, transplanted into the same animal and into other animals fascia which had been kept in an ordinary ice chest at 38 F. for as long as seven days, fascia which had been kept in cold storage at 32 F., wrapped in gauze and moistened with salt solution, for thirty-five days and fascia which

had been kept in cold storage at 32 F. in physiologic solution of sodium chloride for fifty-six days.

In 1911 Dean Lewis and C. B. Davis' experiments demonstrated the difference in end results between transplantation of tendons into subcutaneous tissue and insertion of tendons into tendon defects, so that they had to function early. In the former site the tendon transplant shrank considerably but retained all the physical properties of tendon except for a considerable loss of luster. There was no proliferation of the peritendineum such as occurs in transplants made to function early.

In the past fifteen years fascia has been used successfully in plastic and in orthopedic operations and also in other types of operations. This was probably brought about by the work of Gallie and Le Mensurier, Koontz, Bennett and others.

Mason and Shearon in 1932, in a thorough study of tendon suture and tendon grafts, concluded that in a healing tendon suture union is accomplished first by a proliferation of the sheath tissues, which reestablish continuity in a few days. The tendon begins to proliferate after the fourth or fifth day, sending cells into the callus. With autogenous tendon grafts a similar process of healing was noted, the only difference being that the sheath of the graft and the tendon of the graft remained viable and took part in closing the gap between the separate stumps.

MATERIALS USED TO FILL DEFECTS IN TENDONS

Catgut, silk, silver wire, tendons and fascia have been used in reconstructing tendons.

The use of foreign materials was often complicated by pressure necrosis of the skin. At times the neighboring tissues proliferated, invaded and limited the function of the new tendon. There are some disadvantages in direct transplantation of tendon. In order to prevent dysfunction, the amount of tendon to be used for this purpose must necessarily be small. Preserved tendon is bulky; it tends to curl up and is not very pliable. Its fibers are grouped into stout cords, and vascularization of its deeper structures is somewhat hard to establish.

Fascia is essentially the same kind of tissue as is tendon, but it is thinner. It consists of many parallel layers of heavy white fibrous tissue, between which are situated a few scattered cells. The fibers are arranged in thin sheets and are divided into irregular bundles by areolar tissue, which also covers the surface and in which ramified blood vessels and lymphatics are present. Fascia is an ideal material for transplantation. It is thin and is easily permeated by serum; it has great strength. Loops of fascia fastened in a vise have withstood a weight of 90 pounds (40 Kg.) without breaking, the ends of the fascia slipping from the vise first (Lewis, 1917). It has a tensile strength of 32

pounds and 10 ounces (15 Kg.) per inch in width (Ross) or of 7,860 pounds (3,510 Kg.) per square inch, with an elasticity of well over 91 per cent (Gratz, 1931).

Ox fascia (dead) has been used surgically only in comparatively recent years. Nageotte and Sencert communicated important fundamental knowledge about heterografts. Koontz has made valuable experimental and clinical contributions in this field.

According to Nageotte and Sencert, preserved fascia does not differ essentially from living fascia, because the connective tissue fibers originating from living tissue are inert and are indistinguishable from a dead graft when studied microscopically. If fascia is preserved in alcohol the physical and clinical properties remain the same. The studies of these workers indicated that the dead cells of the graft are removed by wandering cells from the host, after which fibroblasts from the host grow into preexisting connective tissue framework of the graft and repopulate it with living cells. In a short time it becomes impossible to tell that the graft has ever been dead. If this is true there should be no foreign body reaction in the healing of such grafts. Clinically, this has been debated by some. Experimentally, Rosenblatt and Meyers disagreed with this principle. If all biologic laws have been observed and the grafted tissue has been made to function early, absorption should not take place.

The experimental work of Rosenblatt and Meyers indicated that there is some absorption of the graft. Wolfsohn agreed with them.

Haas has studied the mode of union of live and preserved fascia with muscle. He stated that the union is as rapid with one as with the other; that, microscopically, there is no apparent difference. He concluded, however, that live fascia looks more tendinous and less edematous than preserved fascia.

There are two main complications to be considered in the use of dead fascia, namely, infection and foreign body reaction. In reports of large series of cases, in which it has been used clinically by Koontz and others (mainly in the repair of hernias), these complications were negligible.

STATEMENT OF THE PROBLEM

An endeavor was made to determine whether dead fascia (used to fill defects in tendons) will or will not act as a foreign body and whether or not absorption occurs. An attempt was also made to study the factors which enter into the healing of such defects.

TECHNIC OF EXPERIMENTS

Thirty experiments were performed on dogs under general anesthesia. The following technic was employed: One of the tendons in the foreleg was exposed,

and a section was removed from it. A strip of dead (ox) fascia which had been preserved in 70 per cent alcohol was then sutured to the tendon stumps by means of Frisch sutures of black silk (fig. 1). This type of suture was used because it has been shown experimentally by Kimura that it can withstand considerable traction for from three to fifteen hours. It also permits a good approximation and does not strangle the tissues when the tendon moves. In some of the animals the sheath was removed from the host tendon before a portion of it was resected. No casts or other means of immobilization were applied. Five of the animals were not available for study because in 3 the incisions broke down and 2 died of distemper.

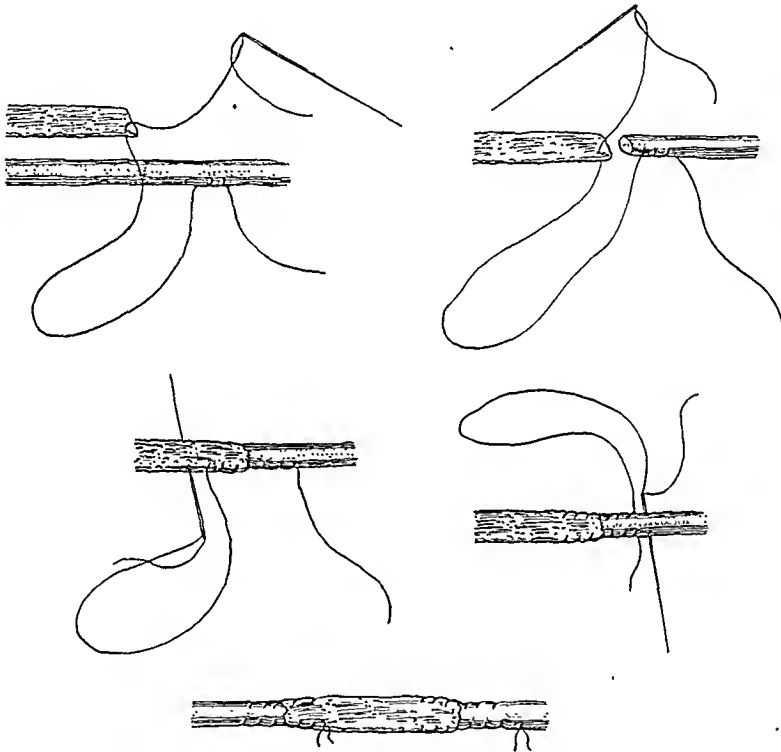


Fig. 1.—Method of suturing used in this series of experiments.

The animals were killed at intervals of eleven, twenty-one, twenty-eight, thirty-five, forty-two, fifty-six, one hundred and fifty, one hundred and eighty, two hundred and forty and two hundred and eighty-five days. The fascial grafts were studied, grossly and microscopically.

PROTOCOLS OF EXPERIMENTS

Dog 1 (killed at eleven days).—The fascia was smooth and glistening. The junction of the tendon and graft was marked by a smooth reddish band. The graft was edematous, but there were no adhesions around it. Microscopic examination showed much edema and also cellular reaction consisting of round cells and polymorphonuclear cells. There were a large number of foreign body giant cells, especially about the silk sutures; young fibroblasts used the silk sutures

as an avenue to work into the graft. The proximal and distal ends of the dead fascia were edematous, frayed and undergoing absorption; they were being split into strands by an ingrowth of fibroblasts. The graft was encircled by young fibroblasts as if in a cylinder. From this outer layer, fibroblasts were seen working into the interior of the graft. The junction of the graft and the tendon was made up of granulation tissue which was fairly dense. The dead fascia, therefore, was not acting as a foreign body.

Dog 2 (killed at twenty-one days).—The sheath of the host tendon was destroyed before the graft was implanted. The graft appeared enlarged and edematous; it was firmly united to the tendon stumps. Microscopic examination

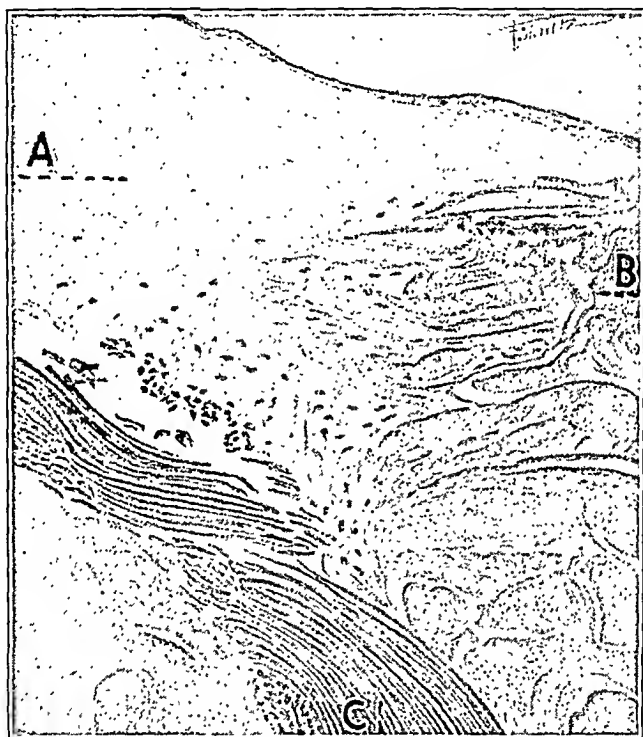


Fig. 2.—Section of graft of dog 1, killed at eleven days. Note the edematous graft broken up into strands by ingrowth of fibroblasts from surrounding granulation tissue. *A* represents an area of granulation tissue; *B*, the graft in process of breaking up; *C*, the silk suture.

revealed the fact that the graft was being invaded by fibroblasts with extremely thin nuclei. These fibroblasts were most marked at the proximal and distal portions of the graft but were seen in the interior of the graft as well. The graft at the proximal end showed a gradual fraying, with definite invasion by granulation tissue and especially by fibroblasts, which were bringing about a gradual transition between the graft and the host tendon. Part of the graft was being absorbed, without the aid of cells, by chemical degeneration. Connective tissue was present in great abundance throughout the region. It was becoming compact and laminated and was arranged almost in bundles, especially about the periphery of the graft.

It was most profuse at the junction of the graft and the tendon. In the granulation tissue the blood supply was good. In the graft the circulation was virtually nonexistent except for capillaries in the newly formed granulation tissue which had permeated the graft. The silk had lost some of its consistency, being broken up and fragmented. The junction between the graft and the tendon was much firmer than in the previous experiment.

DOG 3 (killed at twenty-one days).—The sheath of the host tendon was preserved. Examination showed a much firmer union between the graft and the tendon than was observed in the preceding study, of the same duration, and in which the tendon sheath was destroyed. Many more foreign body giant cells



Fig. 3.—Section of graft of dog 2, killed at three weeks. The tendon sheath was destroyed. Note the fibroblastic invasion of the graft, bringing about a gradual transition between graft and tendon. *A* represents an area of granulation tissue; *B*, the graft; *C*, the silk suture.

appeared about the silk, which was becoming frayed and pigmented. There was also an infiltration of granulation and fibrous tissue about the silk. A considerable amount of new fibrous tissue was present around the graft; this was compact, laminated and cellular, indicating marked activity. The graft was invaded throughout by fibrous tissue.

DOG 4 (killed at twenty-eight days).—The sheath of the tendon was destroyed. Union was firm; the graft was glistening; the edges had become rounded and smooth. There was a slight infection about the silk sutures. Microscopically, the silk was much more fragmented, and large amounts of it had disappeared.

There was marked polymorphonuclear infiltration about the silk. The graft showed a much greater degree of invasion by fibroblasts. In some places the body of the graft was almost displaced by this invasion. The small amount of graft which still had its original architecture intact was flanked on all sides by rows of fibroblasts.

Dog 5 (killed at twenty-eight days).—The tendon sheath was left intact. Around the periphery there was a tremendous amount of proliferation of fibrous tissue, probably coming from the sheath of the host tendon. There was a small amount of silk surrounded by giant cells. The proximal part of the graft showed the greatest degree of infiltration, in other words the most advanced stage of

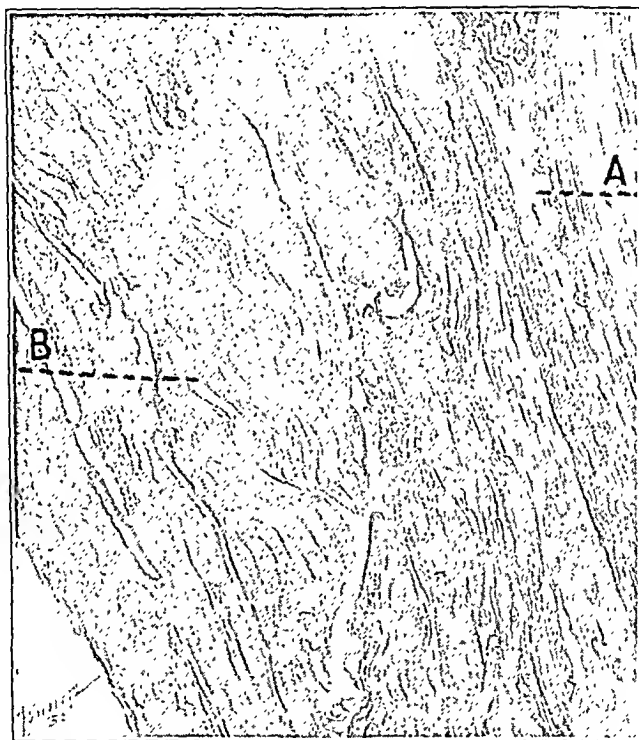


Fig. 4.—Section of graft of dog 3, killed at three weeks. The tendon sheath was left intact. Note the new fibrous tissue about the periphery of the graft, compact, firm, laminated and cellular. It is much more abundant than in the graft shown in figure 3. *A* represents an area of granulation tissue; *B* the tendon graft.

substitution. There were no signs of inflammation, and only slight chemical destruction and absorption had occurred.

Dog 6 (killed at thirty-five days).—The tendon sheath was destroyed. Union was decidedly firm. Microscopically, little of the graft remained. It was almost completely replaced by young laminated fibrous tissue. The silk had become fragmented; there was some foreign body giant cell reaction about it.

Dog 7 (killed at thirty-five days).—The tendon sheath was left intact. A slight infection was noted about the sutures, but the graft was firm, glistening



Fig. 5.—Section of graft of dog 4, killed at four weeks. The tendon sheath was destroyed. Note the much greater degree of invasion of the graft by fibroblasts. *A* represents new tissue invading the graft; *B*, the tendon graft undergoing invasion; *C*, the silk suture.

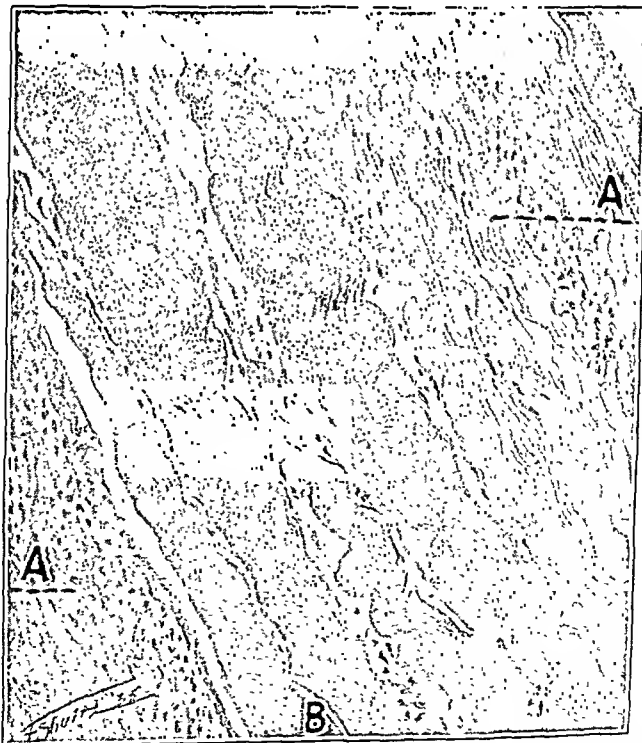


Fig. 6.—Section of graft of dog 5, killed at four weeks. The tendon sheath was left intact. Note the marked amount of fibrous tissue proliferation about the periphery of the graft, probably coming from the sheath. *A* represents granulation tissue; *B*, tendon graft.

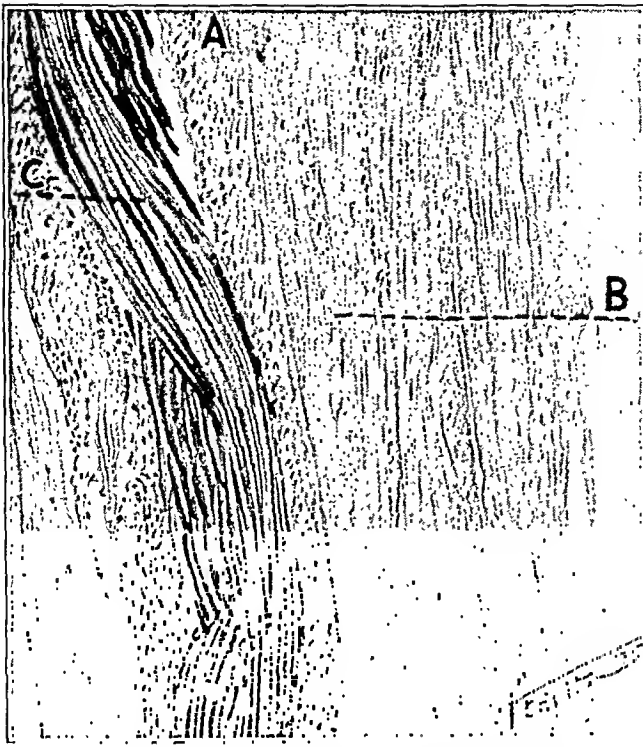


Fig. 7.—Section of graft of dog 6, killed at five weeks. The tendon sheath was destroyed. Note that the graft is almost replaced by young laminated fibrous tissue. *A* represents granulation tissue; *B*, the tendon graft; *C*, the silk suture.



Fig. 8.—Section of graft of dog 7, killed at five weeks. The tendon sheath was left intact. Note that the graft has lost the architectural appearance noted in earlier periods and is almost completely infiltrated by fibrous tissue. *A* represents granulation tissue; *B*, the tendon graft; *C*, the silk suture.

and not adherent to the sheath. No definite evidence of the dead graft remained. There was an almost complete substitution by young fibrous tissue.

Dog 8 (killed at fifty-six days).—The sheath was left intact. Grossly, the graft was indistinguishable from the tendon except for the silk sutures. Microscopically, there was no obvious remnant of the graft. There was a large amount of laminated fibrous tissue arranged in strands.

Dog 9 (killed at one hundred and fifty days).—The sheath was left intact. Grossly, the graft was indistinguishable from the tendon. Microscopically, there had been a complete substitution.

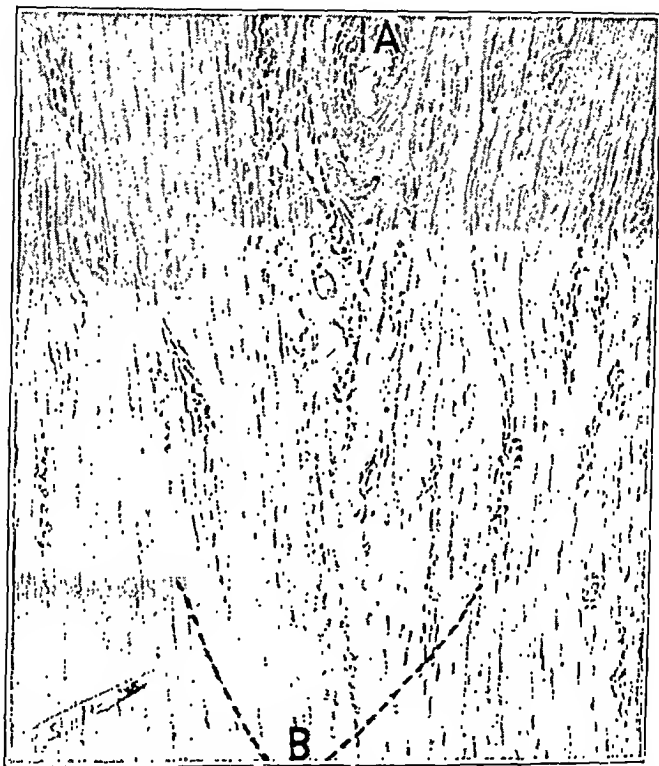


Fig. 9.—Section of graft of dog 8, killed at eight weeks. Note that there is no obvious remnant of the graft. There is a large amount of uniform fibrous tissue arranged in strands and laminated. *A* represents a blood vessel; *B*, the tendon graft.

Dog 10 (killed at one hundred and eighty days).—The sheath was left intact. The graft had not shaped like the others but was smooth, glistening and not adherent to the sheath. Microscopically, some of the dead graft was still present. The degree of permeation was not as extensive as in the others, which may have been due to the fact that the animal was much older than the other subjects. In places, the graft was separated at its periphery from the surrounding structures; this shows that there was motion in the graft.

Dog 11 (killed at two hundred and ten days).—The sheath was left intact. Union was firm; the sutures plainly visible; the graft was gliding nicely in the

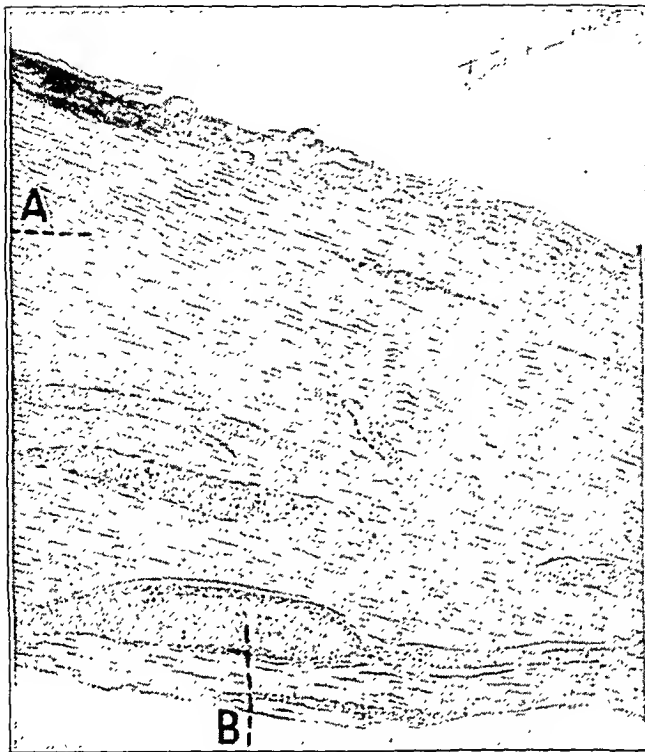


Fig. 10.—Section of graft of dog 9, killed at eight months. Note that no evidence of the graft remains. There is moderately dense fibrous tissue. *A* represents the tendon graft; *B*, a vein.



Fig. 11.—Section of graft of dog 15, killed at eight and one-half months. Note that a cross section through the graft looks like regular tendon in structure. *A* represents the tendon.

sheath. Microscopically, there were no definite signs of the graft. There had been a complete substitution by fibrous connective tissue poor in cellular activity.

Dog 12 (killed at two hundred and forty days).—The sheath was left intact. It became only slightly adherent; the graft was firmly united. It had become rounded and smooth and had acquired the shape of the tendon. Microscopically, there was a considerable amount of dead graft left, but it was flanked on all sides by a large amount of laminated fibrous tissue.

Dog 13 (killed at two hundred and forty days).—The sheath was left intact. There was no evidence of the graft; there was considerable fibroblastic activity.

Dog 14 (killed at two hundred and forty days).—The sheath was left intact. The animal was the largest subject used. The graft was tremendously hypertrophied and lengthened. It was smooth and glistening. Microscopically, the blood supply was better than in the others. There was no evidence of the dead graft; not much cellular reaction was noted; there was moderately dense fibrous tissue.

Dog 15 (killed at two hundred and sixty days).—The sheath was left intact. Microscopically, there were no definite signs of the dead graft; there were large

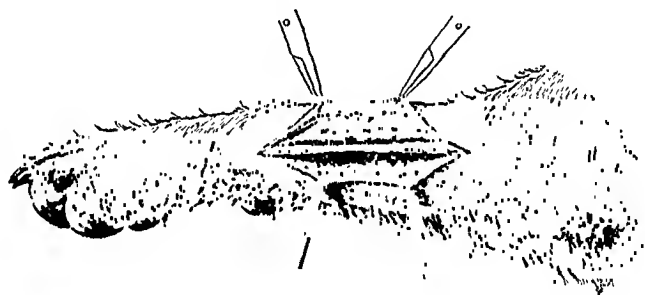


Fig. 12.—End result of the transplant in dog 15.

amounts of loose areolar tissue. The silk had been broken up and was surrounded by fibrous tissue. Cross section showed a regular tendon-like structure.

Dog 16 (killed at two hundred and eighty-five days).—The sheath was left intact. The graft could not be distinguished grossly. Microscopically, there was no evidence of the graft.

SUMMARY

Twenty-five animals were studied, in which tendon defects had been filled with strips of dead (ox) fascia preserved in 70 per cent alcohol. The proximal and distal ends of the graft became frayed and edematous and were invaded by an ingrowth of young fibroblasts. These later worked their way into the interior of the graft, so that as a rule after forty-two days little evidence of the dead graft, as such, remained. A greater degree of fibroblastic activity was noted with the animals in which the tendon sheath was kept intact. This was especially marked about the periphery of the graft and appeared to be the forerunner of the new sheath of the new tendon. As time went on, the new tissue became more compact and laminated.

There was no foreign body giant cell reaction except around the silk sutures. A small amount of absorption was noted, but not enough to have any clinical significance. In other words, the preserved fascia was well tolerated. In time there was such a complete substitution that it was difficult to tell that the graft had ever been dead.

BIBLIOGRAPHY

- Adams, W.: On the Reparative Process in Human Tendons After Subcutaneous Division for the Cure of Deformities, with an Account of the Appearances Presented in Fifteen Post-Mortem Examinations in the Human Subject; Also a Series of Experiments on Rabbits and a Résumé of the English and Foreign Literature of the Subject, London, J. Churchill, 1860.
- Balleuil, L. C., and Jock, W. D.: Transplantation of Fascia in War Surgery, *Ann. Surg.* **68**:1 (July) 1918.
- Bennett, G. E.: The Use of Fascia for the Reenforcement of Relaxed Joints, *Arch. Surg.* **13**:655 (Nov.) 1926.
- Relaxed Knees and Torn Ligaments, and Disability Following Such an Injury, *Proc. Internat. Assemb. Inter-State Post-Grad. M. A., North America* [1930] **6**:351, 1931.
- Bertocchi, A., and Bianchetti, C. F.: Sull'evoluzione degli innesti autoplastici transossei e transarticolari di fascia e di tendine con particolare riguardo alla ricostruzione dei legamenti crociati, *Chir. d. org. di movimento* **7**:225 (June) 1923; abstracted, *J. A. M. A.* **81**:964 (Sept. 15) 1923.
- Black, J. C., and Bonnett, P.: Evolution et traitement des plans des dendon flechisseurs des doigts, *Gaz. d. hôp.* **102**:5, 1929.
- Bunnell, S.: Reconstructive Surgery of the Hand, *Surg., Gynec. & Obst.* **39**:259, 1924.
- Burk, W.: Ersatz intermuskularer Fascienschneiden durch frei transplantierte Fascie, *Zentralbl. f. Chir.* **42**:573, 1915.
- Chironi, P.: Contributo sperimentale ed istologico ai liberi trapianti di fascia, *Policlinico. (sez. chir.)* **28**:93 (March 15) 1921; abstracted, *J. A. M. A.* **76**:1435 (May 21) 1921.
- Cuff, C. H.: A Note on the Surgical Uses of the Fascia Lata, *Brit. M. J.* **1**:494 (April 2) 1921.
- Davis, J. S.: Transplantation of Free Laps of Fascia: An Experimental Study, *Ann. Surg.* **54**:734, 1911; *Bull. Johns Hopkins Hosp.* **22**:372, 1911.
- Delorme, E.: Grafts of Dead Tendons, *Bull. Acad. de méd., Paris* **80**:452 (Nov. 19) 1918; abstracted, *J. A. M. A.* **72**:228 (Jan. 18) 1919.
- Gallie, W. E., and Le Mensurier, A. B.: A Clinical and Experimental Study of the Free Transplantation of Fascia and Tendon, *J. Bone & Joint Surg.* **4**:600 (July) 1922.
- Use of Living Sutures in Operative Surgery, *Canad. M. A. J.* **40**:504, 1929.
- Garlock, J. H.: Repair Processes in Wounds of Tendons, and in Tendon Grafts, *Ann. Surg.* **85**:92 (Jan.) 1927.
- Glasser, S. T.: Ox Fascia (Dead Fascia) Graft, *Am. J. Surg.* **19**:542 (March) 1933.
- Gluck, T.: Ueber Muskel- und Sehnenplastik, *Arch. f. klin. Chir.* **26**:61, 1881.
- Gratz, C. M.: Tensile Strength and Elasticity Tests on Human Fascia Lata, *J. Bone & Joint Surg.* **13**:334 (April) 1931.

- History of Tendon Suture, *Medicine and Literature*, M. J. & Rec. **127**:156 (Feb. 1); 213 (Feb. 15) 1928.
- Use of Fascia in Reconstructive Surgery, *Ann. Surg.* **99**:241 (Feb.) 1934.
- Haas, S. L.: The Union of Grafts of Live and of Preserved Fascia with Muscle, *Arch. Surg.* **23**:571 (Oct.) 1931.
- Henderson, M. S.: Habitual Dislocation of the Shoulder, *J. A. M. A.* **95**:1653 (Nov. 29) 1930.
- Heuck: Ein Beitrag zur Sehnenplastik, *Zentralbl. f. Chir.* **9**:289, 1882.
- Kanavel, A. B.: Transplantation of Fat, Living Tissue and Fascia in Surgery; Report of Experiences in Various Conditions, *J. Missouri M. A.* **14**:333 (Aug.) 1917.
- Kirschner, M.: Ueber freie Sehnen- und Fascientransplantation, *Beitr. z. klin. Chir.* **65**:472, 1909.
- Die praktischen Ergebnisse der freien Fascientransplantation, *Arch. f. Klin. Chir.* **112**:888, 1910.
- Die freie Transplantation von Faszien, *Therap. Monatsh.* **25**:711, 1911.
- Der gegenwärtige Stand und die nächsten Aussichten der autoplastischen, freien Fascienübertragung, *Beitr. z. klin. Chir.* **76**:5 and 149, 1913.
- Kleinschmidt, O.: Die freie autoplastische Fascientransplantation, *Ergebn. d. Chir. u. Orthop.* **8**:207, 1914.
- Koch, S. L.: Complicated Contractures of the Hand: Their Treatment by Freeing Fibrosed Tendons and Replacing Destroyed Tendons with Graft, *Ann. Surg.* **98**:546 (Oct.) 1933.
- Koontz, A. R.: Experimental Results in the Use of Dead Fascia Grafts for Hernia Repair, *Ann. Surg.* **83**:523 (April) 1926.
- Dead (Preserved) Fascia Grafts for Hernia Repair, *J. A. M. A.* **89**:1230 (Oct. 8) 1927.
- Healing in Hernia Repair, *Internat. S. Digest.* **4**:195 (Oct.) 1927.
- Muscle and Fascia Suture with Relation to Hernia Repair, *Surg., Gynec. & Obst.* **42**:222 (Feb.) 1926.
- Kornow, P.: Ueber die freie Fascientransplantation: Experimentelle und klinische Untersuchungen, *Beitr. z. klin. Chir.* **65**:144, 1913.
- Lewis, D.: Fascia and Fat Transplantation, *Surg., Gynec. & Obst.* **24**:129, 1917.
- Tendon Injuries: Postoperative Treatment, *Boston M. & S. J.* **194**:913, 1926.
- and Davis, C. B.: Experimental Direct Transplantation of Tendons and Fascia, *J. A. M. A.* **57**:540 (Aug. 12) 1911.
- McArthur, L. L.: Autoplastic Suture in Hernia, and Other Diastases: Preliminary Report, *J. A. M. A.* **37**:1162 (Nov. 2) 1901.
- Autoplastic Suture in Hernia, and other Diastases: Final Report, *ibid.* **43**:1039 (Oct. 8) 1904.
- Mainzer, M.: Ueber indirekte Sehnenüberpflanzung, *München. med. Wchnschr.* **49**:869, 1902.
- Mason, M. L., and Shearon, C. G.: Process of Tendon Repair, *Arch. Surg.* **25**:615 (Oct.) 1932.
- Milch, H.: Repair of Ruptured Quadriceps by Free Fascial Graft Transplant, *J. Bone & Joint Surg.* **13**:361 (April) 1931.
- Monod: Plais des tendons Greffe tendineuse, *Bull. et mém. Soc. de chir. de Paris* **13**:397, 1887; abstracted, *Centralbl. f. Chir.* **14**:959, 1887.
- Morestin, H.: Quelques cas de Greffes graisseuses ophiées à la chirurgie réparatrice, *Bull. et mém. Soc. d. chirurgiens de Paris* **40**:1631, 1915.

- Nageotte, J.: Quelques considerations historiques, au sujet des greffes mortes, *Compt. rend. Soc. de biol.* **72**:615, 1919.
- Quelques considerations sur la greffe, *Presse méd.* **28**:626, 1920.
- Toxicité de certaines greffons morts hétérogènes, *Compt. rend. Acad. d. sc.* **180**:1523, 1920.
- and Sencert, L.: Réparation suivie de succès, par notre méthode "des greffes mortes" de grandes pertes de substance des tendons fléchisseurs des doigts de la main gauche chez un blessé de guerre, *Bull. Acad. de méd., Paris* **80**:448, 1918.
- Patterson, R. H.: Internal Fixation of Fractures and Dislocations, by Use of the Human Fascial Suture, *Ann. Surg.* **88**:879 (Nov.) 1928.
- Peyrot: Transplantation chez l'homme d'un tendon emprunté à un chien, *Bull. et mém. Soc. de chir. de Paris* **12**:356, 1886; abstracted, *Centralbl. f. Chir.* **14**:392, 1887.
- Regard, G. L.: Traitement des paralysies definitives par la greffe de tendons morts, *Rev. méd. de la Suisse rom.* **43**:364, 1923.
- Rehn, E.: Die homoplastische Sehnentransplantation in Tierexperiment, *Beitr. z. klin. Chir.* **68**:417, 1910.
- Zu den Fragen der Transplantation, Regeneration und ortseinsetzenden funktionellen Metaplasie, *Arch. f. klin. Chir.* **112**:662, 1919.
- Rosenblatt, M. S., and Meyers, M.: Muscle Fascia Suture with Preserved Fascia and Tendon, *Surg., Gynec. & Obst.* **47**:836, 1928.
- Royle, N. D.: Living Suture in Tendon Transplantation, *M. J. Australia* **1**:333 (April 5) 1924.
- Saloman, A.: Klinische und experimentelle Untersuchungen über Heilung von Sehnenverletzungen insbesondere innerhalb der Sehnenscheiden, *Arch. f. klin. Chir.* **129**:397, 1924.
- Stewart, F. T.: Fascia and Fat Transplantations, *Surg., Gynec. & Obst.* **24**:141 (Feb. 17) 1917.
- Valentin, B.: Histologische Untersuchungen zur freien Fascientransplantation, *Deutsche Ztschr. f. Chir.* **113**:398, 1911-1912.
- Experimentelle Untersuchungen zur homöoplastischen Fascientransplantation, *Beitr. z. klin. Chir.* **85**:574, 1913.
- Von Eherts, E. M.: Free Transplantation of Fascia, *Surg., Gynec. & Obst.* **18**:318, 1914.
- Wolfsohn, G.: Use of Fibers of Animal Fascia, *Arch. f. klin. Chir.* **147**:479, 1927.

CONGENITAL ANOMALIES OF THE GENITALIA ASSOCIATED WITH UNILATERAL RENAL AGENESIS

WITH PARTICULAR REFERENCE TO TRUE UNICORNUATE UTERUS
REPORT OF CASES AND REVIEW
OF THE LITERATURE

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Since the middle of the last century a number of authors have called attention to the frequent association of congenital anomalies of the genitalia and anomalies of the urinary tract. The numerous reports, however, of cases of genital malformation in which no urologic investigation has been carried out and of cases of congenital renal defect in which adequate study of the genital system has not been made are evidence of the need for reemphasis of the problem. It is my purpose to review the literature and to present 3 illustrative cases; the first is an instance of true uterus unicornis; the second, a case of uterus bicornis bicollis, and the third, an example of uterus bicornis unicollis. In each of these there was total agenesis of one kidney and ureter.

True uterus unicornis is an unusual abnormality, and its combination with renal agenesis is a defect of considerable rarity. I have been able to find reported in the literature a total of less than 30 such cases, and in only a few of these was the diagnosis established before autopsy. The first authentic case is that of Puech,¹ reported in 1855. Kussmaul² in his classic volume of 1859 cited as an example of true unicornuate uterus and renal agenesis a case reported by Chaussier (1817), and almost all subsequent reviewers have incorrectly included this. The anomaly was in reality a unicornuate uterus with an ectopic kidney on the defective side.³ Two other cases are attributed to Rokitsansky.⁴ Paltauf⁵ added

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1. Puech, A.: Note sur les anomalies des organes génitaux, *Compt. rend. Acad. d. sc.* **41**:643, 1855.

2. Kussmaul, A.: Von dem Mangel, der Verkümmerng und Verdopplung der Gebärmutter, Würzburg, Stahel, 1859, pp. 108-168.

3. Chaussier: *Bull. Fac. de méd. de Paris* **5**:436, 1817.

4. Rokitsansky, cited by Eismayer, G.: Ueber Uterusmissbildung bei kongenitem Mangel einer Niere, *Ztschr. f. urol. Chir.* **11**:191 (Jan.) 1923.

5. Paltauf, A.: Zur Kenntnis des Uterus unicornis, *Med. Jahrb. d. k.-k. Gesellsch. d. Aertze Wien*, 1885, pp. 211-256.

another case in 1885; Winckel⁶ added 2 cases in 1890, Brackenbury⁷ 1 case in 1891 and Urban⁸ 2 cases in 1899. Single cases have been described by Naumann,⁹ Délaginière,¹⁰ Pestalozza,¹¹ Alglove,¹² McCrae¹³ Tschischtowitsch,¹⁴ Guthrie and Wilson,¹⁵ Boehme,¹⁶ Rosenthal¹⁷ and Oehler.¹⁸ Guizetti and Pariset¹⁹ contributed 4 such cases, and Schilling²⁰ added 2. In Eismayer's²¹ excellent review is also listed the case of Buhl which had been cited by Paltauf. Paltauf apparently did not, however, consider the uterus in this case a true unicornuate uterus. Two recent instances are those reported by Dannreuther²² and Duncan.²³ Available data on the 27 cases mentioned are presented in the accompanying table. I have been unable to examine the original reports of

6. Winckel, F.: *Lehrbuch der Frauenkrankheiten*, Leipzig, S. Hirzel, 1890, pp. 293-294.

7. Brackenbury, H. B.: Suppression of Urine in a Case of Single Kidney, with an Unusual Malformation of the Generative Organs, *Lancet* 2:869, 1891.

8. Urban: *Berl. klin. Wchnschr.* 36:312, 1899.

9. Naumann, cited by Eismayer, G.: Ueber Uterusmissbildung bei kongenitalem Mangel einer Niere, *Ztschr. f. urol. Chir.* 11:191 (Jan.) 1923.

10. Délaginière, cited by Bolaffio, M.: Zur Kenntnis der kombinierten Missbildung des Harn- und Geschlechtsapparates beim Weibe, *Ztschr. f. Geburtsh. u. Gynäk.* 68:261, 1911.

11. Pestalozza, cited by Bolaffio, M.: Zur Kenntnis der kombinierten Missbildungen des Harn- und Geschlechtsapparates beim Weibe, *Ztschr. f. Geburtsh. u. Gynäk.* 68:261, 1911.

12. Alglove, P.: Malformation congénitale de l'utérus et des annexes du côté droit; uterus unicorne avec ovaire droit en ectopie dans la fosse iliaque droite, *Bull. et mém. Soc. anat. de Paris* 80:652, 1905.

13. McCrae, J.: Unilateral Congenital Absence of the Paired Genito-Urinary Organs, *Montreal M. J.* 37:177, 1908.

14. Tschischtowitsch, cited by Eismayer.²¹

15. Guthrie, D., and Wilson, L. B.: Congenital Unilateral Absence of the Urogenital System, *Ann. Surg.* 50:907, 1909.

16. Boehme, M.: Zwei Fälle von abnormer Ausmündung bzw. Endigung der Ureteren mit besonderer Berücksichtigung der Symptome, *Inaug. Dissert.*, Leipzig, B. Georgi, 1912.

17. Rosenthal, S.: Ueber die kombinierten Nieren-Uterusmissbildungen, *Inaug. Dissert.*, Heidelberg, T. Berkenbusch, 1913.

18. Oehler, F.: Beitrag zur Kasuistik des kongenitalen Nierendefekts und kongenitalen Nierendystopie, *Beitr. z. klin. Chir.* 89:223, 1914.

19. Guizetti, P., and Pariset, F.: Beziehungen zwischen Missbildungen der Nieren und der Geschlechtsorgane, *Virchows Arch. f. path. Anat.* 204:372, 1911.

20. Schilling, F.: Vier Fälle von Uterus unicornis mit gleichzeitiger anormaler oder fehlender Anlage einer Niere, *Inaug. Dissert.*, Leipzig, 1917.

21. Eismayer, G.: Ueber Uterusmissbildung bei kongenitalem Mangel einer Niere, *Ztschr. f. urol. Chir.* 11:191 (Jan.) 1923.

22. Dannreuther, W. T.: Dextroversion of the Uterus, with Congenital Absence of the Left Fallopian Tube, Ovary, Broad Ligament, Round Ligament, Kidney and Ureter, *Am. J. Obst. & Gynec.* 6:51 (July) 1923.

23. Duncan, I. G., in discussion on Gutierrez, R.: Surgical Aspects of Renal Agenesis, *Arch. Surg.* 27:686 (Oct.) 1933.

Data on Case of True Unicornuate Uterus with Unilateral Renal Agenesis

Case No.	Author	Uterus Unicornis Agenesis	Renal	Ureter	Adnexae on Developed Side	Adnexae on Defective Side	Age	Comment
1	Puech (1855)	R	L	Ovary in lumbar region; round ligament unconnected with uterus	15 days	10 pregnancies
2	Rokitansky	L	R	76	
3	Rokitansky	L	R	61	
4	Palfauf (1855)	L	R	R	Normal	Ovary long, in lumbar region; ovarian ligament extending toward inguinal ring; only ostial end of tube; round ligament present		
5	Winckel (1890)	R	L	L	Normal	Round ligament absent		
6	Winckel (1890)	L	R	R	Normal	Ovary and tube solid and rudimentary; broad ligament absent		
7	Brackenbury (1891)	R	L	L	Normal	Small rudimentary ovary above pelvic brim; no tube; broad and round ligaments rudimentary	26	2 miscarriages; menses scanty and painful
8	Naumann	R	L	L	12 hr.	
9	Déjardinère	L	R	Tube and ovary absent		
10	Pastalozza	L	R	R	Tube and ovary absent		
11	Urban (1899)	L	R	Tube and ovary absent		
12	Algrave (1905)	?	?	Ectopic ovary		
13	McCrac (1908)	R	L	L	40	
14	Tschischowitsch (1908)	R	L	L	Tube, ovary and broad ligament absent		
15	Guthrie and Wilson (1909)	R	L	L	Cystic ovary	Tube, ovary and broad ligament absent	30	No menses; monthly cramps
16	Gulzetti and Pariset (1911)	R	L	L	Normal	Tube, ovary and almost all broad ligament absent; round ligament attached to cervix	Term fetus	
17	Gulzetti and Pariset	R	L	L	Normal	Ovary and ostial end of tube 1.5 cm. long; rudimentary broad ligament; round ligament attached to cervix	11 mo.	
18	Gulzetti and Pariset	R	L	L	Ovary 9 cm. long	Ovary 6 cm. long; only ostial end of tube...	44	
19	Gulzetti and Pariset	R	L	L	Normal	Ovary normal; ostial end of tube; both in inguinal hernia; only lower half of broad ligament; round ligament attached to cervix	43	
20	Gulzetti and Pariset	R	L	L	Ovary 2 cm. long	Ovary 2.3 cm. long; only ostial end of tube, 2 cm. long; only lower portion of broad ligament; round ligament attached to cervix	56	
21	Boehme (1912)	R	L	L	Ovary in front of internal inguinal ring		
22	Rosenthal (1913)	R	L	L	Ectopic ovary and tube		
23	Oehler (1914)	R	L	L	Normal	Atrophic tube and ovary lying in hernial sac without connection to uterus; vessels from aorta and vena cava; broad and round ligaments absent	59	
24	Schilling (1917)	L	R	R	Ectopic ovary	Ovary long; incompletely descended; only ostial end of tube; ovarian ligament and mesosalpinx fused with peritoneum of processus vaginalis; round ligament rudimentary	1 day	
25	Schilling	L	R	R	Normal	Ovary above linea innominata; only ostial end of tube	2½ days	
26	Dauencourther (1923)	R	L	L	Normal	Ovary, tube and round and broad ligaments absent	25	2 miscarriages; 1 term pregnancy
27	Duncan (1923)	R	L	L	Ovary and tube absent	26	
28	Shumacker	L	R	R	Ectopic ovary and tube; only ostial end of tube; no broad ligament	13	

6 of these. Not listed are 2 other possible instances, reported by Campbell²⁴ and Collins,²⁵ both examples of renal agenesis and unicornuate uterus diagnosed at autopsy. In the report of neither of these, however, is it stated whether the anomaly was a true unicornuate uterus or the so-called unicornuate uterus with a rudimentary second horn. In all the cases mentioned except those of Dannreuther, Duncan, and Guthrie and Wilson the diagnosis was apparently made at autopsy and not by clinical and surgical observations during life. In the first 2 of these 3 cases pyelograms were not obtained, but findings at laparotomy and at cystoscopic examination gave convincing evidence of renal and ureteral agenesis.

The patients in the cases tabulated varied in age from one day or less²⁶ to 76 years.² The defective development was on the left side in about 60 per cent of cases. In 9 instances the ovary and tube were described as completely absent on the defective side.²⁷ The ovary was ectopic in 11 others,²⁸ usually lying above the pelvic brim. In 2 instances it lay in an inguinal hernial sac.²⁹ In 2 the ovary was described as small, rudimentary or immature.³⁰ Paltauf⁵ has pointed out, however, that in general the ovary on the defective side of a uterus unicornis (with or without a rudimentary second horn) is likely to be longer, though perhaps narrower, than the ovary on the normally developed side. Such was the finding in the case of my patient. The fallopian tube when present at all on the defective side is almost invariably only a short portion of the fimbriated end. The round ligament was absent in 3 instances.³¹ It is usually present, however, as a small, poorly developed structure attached to the cervical portion of the uterus. In 1 case it was said to have no connection with the uterine body.¹ Winckel stated that the broad ligament is absent on the defective side, and this is certainly true in general. In a few instances the ligament was described as present but only as a thin remnant of the lower portion.¹⁹ Where an adequate description is given the ovarian ligament is said to extend down toward or into the internal inguinal ring. In cases in which the

24. Campbell, M. F.: Congenital Unilateral Absence of One Kidney: Unilateral Renal Agenesis, *Ann. Surg.* **88**:1039 (Dec.) 1928.

25. Collins, D. C.: Congenital Unilateral Renal Agenesis, *Ann. Surg.* **95**:715 (May) 1932.

26. (a) Naumann.⁹ (b) Guizetti and Pariset.¹⁹ (c) Schilling.²⁰

27. (a) Urban.⁸ (b) Délaginière.¹⁰ (c) Pestalozza.¹¹ (d) McCrae.¹² (e) Tschischtowitsch.¹⁴ (f) Guthrie and Wilson.¹⁵ (g) Guizetti and Pariset.¹⁹ (h) Dannreuther.²² (i) Duncan.²³

28. (a) Puech.¹ (b) Paltauf.⁵ (c) Brackenbury.⁷ (d) Alglave.¹² (e) Guizetti and Pariset.¹⁹ (f) Boehme.¹⁶ (g) Rosenthal.¹⁷ (h) Oehler.¹⁸ (i) Schilling.²⁰ (j) Shumacker, this paper.

29. (a) Oehler.¹⁸ (b) Guizetti and Pariset.¹⁹

30. (a) Winckel.⁶ (b) Oehler.¹⁸

31. (a) Winckel.⁶ (b) Oehler.¹⁸ (c) Schilling.²⁰

origin of the ovarian vessels has been traced they have been found to arise directly from the aorta and the vena cava. The external genitalia are almost invariably normal, although occasionally malformed.³² Other congenital anomalies sometimes occur in association with this condition.

With true unicornuate uterus the menses may be normal, or they may be scanty, irregular and painful. As early as 1859, Kussmaul² pointed out that pregnancy and delivery may occur with this anomaly, and he cited 4 cases in which 14 pregnancies were reported. Chaussier's patient³ alone had 10 pregnancies. In a number of cases spontaneous abortions occurred³³ but it is impossible from the data available to state whether unicornuate uterus predisposes to abortion. Birk³⁴ had a patient with unicornuate uterus who had three consecutive breech deliveries.

Some idea as to the relative frequency of this abnormality and that of the various other congenital anomalies occurring in females is obtained from the report of Pfleiderer.³⁵ During a period of twenty years 93 instances of genital anomalies were seen at the Tübingen Frauenklinik. There were 14 instances of rudimentary solid uterus with a solid vagina, 6 of uterus unicornis with a rudimentary horn, 15 of uterus bicornis bicollis with a double or single vagina, 15 of uterus bicornis unicollis, 16 of uterus septus with a double or single vagina and 27 of uterus arcuatus. There was no case of true unicornuate uterus.

Thus far only true unicornuate uterus has been considered. The so-called unicornuate uterus with a rudimentary second horn is met with much more commonly and is likewise frequently associated with unilateral renal agenesis. Kussmaul² collected reports of 5 such cases from the literature; Ballowitz³⁶ 12, and Bolaffio³⁷ collected 19. It is, however, frequently difficult to ascertain from the description in the literature whether the given case was one of uterus unicornis with a rudimentary horn on the defective side or one of uterus bicornis with a rudimentary horn. Eismayer²¹ listed all these previously cited cases under the general heading of uterus bicornis cum rudimento cornus unius lateris and described the uterus in all but 4 of them as definitely bicornuate. He

32. (a) Winckel.⁶ (b) Guthrie and Wilson.¹⁵ (c) Guizetti and Pariset.¹⁹

33. (a) Brackenbury.⁷ (b) Dannreuther.²²

34. Birk, J. W.: Pregnancy in Uterus Unicornis, Illinois M. J. 59:30 (Jan.) 1931.

35. Pfleiderer, A.: Ueber Gebärmuttermissbildungen, Monatschr. f. Geburtsh. u. Gynäk. 82:401 (Aug.) 1929.

36. Ballowitz, E.: Ueber angeborenen, einseitigen, vollkommenen Nierenmangel, Virchows Arch. f. path. Anat. 141:309, 1895.

37. Bolaffio, M.: Zur Kenntnis der kombinierten Missbildungen des Harn- und Geschlechtsapparates beim Weibe, Ztschr. f. Geburtsh. u. Gynäk. 68:261, 1911.

added from the literature reports of 11 similar cases. Jung³⁸ and Pfeleiderer³⁵ have recently reported additional examples.

Unicornuate or bicornuate uterus with a rudimentary horn is, then, similar to true unicornuate uterus in its frequent association with solitary kidney. Additional complications, however, may accompany these anomalies, which are not met with in cases of true unicornuate uterus, namely, (1) hematosalpinx and hematometra on the rudimentary side and (2) pregnancy in the rudimentary horn. Paltauf⁵ collected reports of 23 cases of pregnancy in the rudimentary horn, in which the condition was observed at autopsy. In 14 cases rupture had occurred. Pregnancy with rupture is a rather frequent occurrence. Lantuéjoul³⁹ recently reported such a case, in which death occurred from rupture.

Unilateral renal agenesis is also found in association with various other anomalies of the female genital tract. Eismayer²¹ collected from the literature reports of 7 cases in which it occurred in association with a defect or maldevelopment of one tube or absence of one tube and ovary. In general, it may be stated that when renal agenesis occurs in cases of genital anomaly with unilateral defective development, the kidney is always absent on the same side with the genital defect.

Renal agenesis occurs in association with symmetric genital anomalies as well as with unilateral defects. Eismayer²¹ found 18 cases in which the condition occurred in association with rudimentary genital development on both sides. Among these were instances of complete absence of the vagina, the uterus and the tubes. A recent case of this type was reported by Adams.⁴⁰ Of particular importance is the occurrence of solitary kidney in patients with the relatively common types of double uterus. Although the patients in many reported cases of double uterus were not subjected to any urologic investigation, there is good reason to believe that double uterus is rather frequently associated with unilateral renal agenesis. Eismayer²¹ collected reports of 40 such cases in 1923. In 3 of these the defect was extremely slight (uterus septus or bilocularis). Cosgrove and Waters⁴¹ and van Gelderen⁴² have recently

38. Jung, M.: Ueber den Begriff des Uterus pseudounicornis, *Monatschr. f. Geburtsh. u. Gynäk.* **75**:131 (Nov.) 1926.

39. Lantuéjoul, P.: Utérus unicorne avec corne accessoire rudimentaire; grossesse dans la corne rudimentaire; rupture spontanée, *Bull. Soc. d'obst. et de gynec.* **21**:170 (March) 1932.

40. Adams, E. A.: Report of a Case of Congenital Single Kidney with Associated Absence of Uterus and Vagina, *New England J. Med.* **200**:1037 (May 16) 1929.

41. Cosgrove, S. A., and Waters, E. G.: Eclampsia in a Patient with a Duplex Uterus and a Single Kidney, *Am. J. Obst. & Gynec.* **9**:360 (March) 1925.

42. van Gelderen, C.: Agenesia renis, Uterus bicornis duplex, Vagina septa resp. subsepta, *Beitr. z. path. Anat. u. z. allg. Path.* **81**:213 (Nov. 28) 1928.

reported instances of double uterus associated with a single kidney. My second and third cases illustrate this type of congenital malformation.

Renal agenesis is not the only abnormality of the urinary tract found in association with uterus unicornis and the other malformations of the genital tract. I have previously referred to the early case of Chaussier.³ Paltauf⁵ also reported a case of true unicornuate uterus associated with an ectopic pelvic kidney on the defective side. Bolaffio³⁷ found in his review of combined renal and genital abnormalities 1 case of true unicornuate uterus in which the anomaly was associated with a rudimentary kidney and 12 in which it was associated with renal agenesis. Uterus unicornis with a rudimentary horn, was found in association with a rudimentary kidney in 1 case, with an ectopic kidney in 8 cases and with a solitary kidney in 19 cases. A double separate uterus with a double vagina and an ectopic kidney were present in 1 case. A rudimentary uterus, wholly or partially solid, was found in association with an ectopic kidney in 16 cases and a solitary kidney in 10 cases. Uterus bicornis septus or subseptus was associated in 6 instances with a rudimentary kidney, in 3 with an ectopic kidney and in 25 with a solitary kidney. Of the cases of uterus introrsum, arcuatus and planifundalis, septus, subseptus and simplex, a rudimentary kidney was found in 2, an ectopic kidney in 3 and a solitary kidney in 3. Guizetti and Pariset¹⁹ reported an instance of fused kidney associated with uterus bicornis unicollis. They had 3 male and 2 female patients with congenital malformation of the genitalia, associated with an ectopic kidney.

It is exceedingly difficult to estimate the percentage of patients in whom renal agenesis is associated with unicornuate uterus or with other genital anomalies, because of the lack of investigation of the urinary tract in many of the reported cases. More data are available concerning the incidence of genital anomalies among patients presenting unilateral renal agenesis.

One of the first authors to collect a large series of cases was Ballo-witz,³⁶ who found 210 cases reported in the literature, to which he added 3 of his own. Genital defects were more common in females (41 instances in 71 females) than in males (28 instances in 113 males). Among the 41 females with anomalies of the genitalia were 5 with true unicornuate uterus and 13 with unicornuate (or bicornuate) uterus with a rudimentary horn.

A number of other authors who have subsequently reviewed the literature or have presented the results of series of autopsies are Radasch,⁴³

43. Radasch, H. E.: Congenital Unilateral Absence of the Urogenital System and Its Relation to the Development of the Wolffian and Müllerian Ducts, *Am. J. M. Sc.* **136**:111, 1908.

Anders,⁴⁴ Guizetti and Pariset,¹⁹ Dorland,⁴⁵ Eisendrath,⁴⁶ Goldstein,⁴⁷ MacKenzie and Hawthorne,⁴⁸ Campbell,²⁴ Collins²⁵ and Gutierrez.⁴⁹ Anders added 61 cases from the Philadelphia hospitals to the 225 reported cases of "genuine single kidney." Of his own cases, descriptions of the genitalia were available for 27, in 19 of which some congenital anomaly existed. Of the entire 286, data were available on 135, in 94 of which some congenital defect of the genitalia was present (40 males, 49 females and 5 patients whose sex was not stated). Guizetti and Pariset¹⁹ encountered unilateral renal agenesis 39 times among 20,000 autopsies at Parma. There was a complete description of the genital organs of only 8 of the 27 males. Only 1 of the 8, however, showed normal development of the genitalia. The most common anomaly in his series as well as in other series reported was absence of the ductus deferens, the seminal vesicle and the ejaculatory duct on the side on which the kidney was absent and sometimes, in addition, absence of the body and tail of the epididymis. Eight of the 12 females had some genital malformation. Two lacked the vagina and the uterus, 1 had a uterus bicornis unicollis and 5 had true uterus unicornis. Of Campbell's²⁴ patients, 1 of 5 males and 2 of 4 females showed anomalies of the genital organs. Collins²⁵ listed a total of 581 cases. Nearly 90 per cent of the females and about one fourth of the males had anomalies of the genitalia. Gutierrez,⁴⁹ Eisendrath⁴⁶ and others expressed the belief that cases other than those in which the condition was true renal agenesis have been included in most of the reviews, and Gutierrez estimated that from 30 to 40 per cent of the reported cases should be excluded. He agreed with others that the incidence of genital anomalies associated with solitary kidney is high and that it is higher in females (about 70 per cent) than in males. He estimated that the incidence of true renal agenesis in a series of 92,690 reported autopsies was about 1 in 1,600.

44. Anders, J. M.: Congenital Single Kidney with Report of a Case: The Practical Significance of the Condition with Statistics, *Am. J. M. Sc.* **139**: 313, 1910.

45. Dorland, W. A. N.: A Consideration of Renal Anomalies, *Surg., Gynec. & Obst.* **13**:303, 1911.

46. Eisendrath, D. N.: Congenital Solitary Kidney, *Ann. Surg.* **79**:206 (Feb.) 1924.

47. Goldstein, A. E.: Congenital Absence of One Kidney, with a Review of the Literature and Report of Two Cases, *South. M. J.* **18**:750 (Oct.) 1925.

48. MacKenzie, D. W., and Hawthorne, A. B.: Unilateral Renal Aplasia, *Surg., Gynec. & Obst.* **46**:42 (Jan.) 1928.

49. Gutierrez, R.: Surgical Aspects of Renal Agenesis, with Special Reference to Hypoplastic Kidney, Renal Aplasia and Congenital Absence of One Kidney, *Arch. Surg.* **27**:686 (Oct.) 1933.

REPORT OF CASES

CASE 1.—*Left uterus unicornis; right renal and ureteral agenesis; abnormal umbilical ligament.*

D. W., a girl aged 13, was admitted to the hospital on Feb. 20, 1937, complaining of abdominal pain, nausea and vomiting of eight hours' duration.

She had felt entirely well the preceding day and had eaten nothing unusual. About 5 a. m. on the day of admission she was awakened with mild cramps in the lower part of the abdomen. Shortly afterward she passed a normal stool; then she became nauseated and vomited. She vomited again an hour later after taking sodium bicarbonate and again at noon after drinking a glass of milk. The vomitus contained no blood. She had three additional stools during the day; they were all soft, formed and brown, without blood or mucus. The cramplike pains in the lower part of the abdomen gradually grew more severe until a half hour before admission, when they became milder. There remained a diffuse soreness of the lower part of the abdomen. There was never any definite localization on one side or the other. She had marked anorexia. She presented no cardio-respiratory or genitourinary symptoms.

The family history included no report of congenital or familial diseases.

The patient had enjoyed good health, although her parents had always considered her a delicate child. She had had a number of the usual childhood diseases, including scarlatina. A review of systems did not reveal anything remarkable. She had never had an attack similar to the present one, but had had fairly frequent attacks of "indigestion" which she associated with dietary indiscretion. These were characterized by epigastric distress, severe headache and occasionally nausea and vomiting. They always subsided within an hour or so with no treatment beyond rest in bed. The bowels moved regularly two or three times daily; the stool was always normal in color and consistency. She had had considerable difficulty in overcoming enuresis, but had corrected it several years previously by being awakened to urinate at certain intervals during the night, since which time she had had nocturia one or two times. Occasionally she had some urgency to urinate, and if micturition were delayed she would sometimes void incontinently. There were no other urinary symptoms. She had never menstruated.

Examination revealed a nervous, apprehensive child, a little underdeveloped for her years. She was uncomfortable but in no great pain. The face was flushed; the skin was warm and moist. The chief center of interest was the abdomen. It was of normal contour, without distention, visible mass or peristaltic waves. The umbilicus was normal in appearance. There was tenderness to moderate pressure in both lower quadrants, consistently more on the right side than on the left and constantly maximal directly over McBurney's point. Although there was no involuntary spasm, there was a tendency during palpation to splinting of the right lower quadrant and not of the left. There was no cutaneous hyperesthesia and no evidence of irritation of the psoas or obturator muscles. The external genitalia were normal; the vaginal outlet was virginal. During rectal examination the patient complained bitterly, and she cooperated so poorly that it was impossible to ascertain whether there was any real pelvic peritoneal sensitivity. No mass was felt. Bimanually, the internal genitalia were not palpable, but no particular significance was attached to this preoperatively because the examination was so unsatisfactory. The urine was normal. The erythrocyte count was 5,980,000, and the hemoglobin content 97 per cent. The leukocyte count was 11,500, with 84 per cent polymorphonuclears (27 per cent nonsegmented), 6 per cent lymphocytes, 8 per cent mononuclears, 1 per cent eosinophils and 1 per cent

basophils. The Kahn test gave a negative reaction. The blood was of group I (Jansky). The temperature was 101.4 F.; the pulse rate, 112; the respiratory rate, 20, and the blood pressure, 112 systolic and 86 diastolic.

Although the history and findings were certainly not typical, it was felt that the picture was sufficiently suggestive of acute appendicitis to make laparotomy advisable.

A low right rectus incision was made. No free fluid was seen when the peritoneum was opened. The appendix was normal in appearance; the cecum and ascending colon presented no abnormality; the ileum showed nothing unusual; Meckel's diverticulum was not seen, and there was no mesenteric adenitis. There was an extraordinary umbilical ligament which divided the pelvis almost completely into two parts. Its upper border was attached to the anterior abdominal

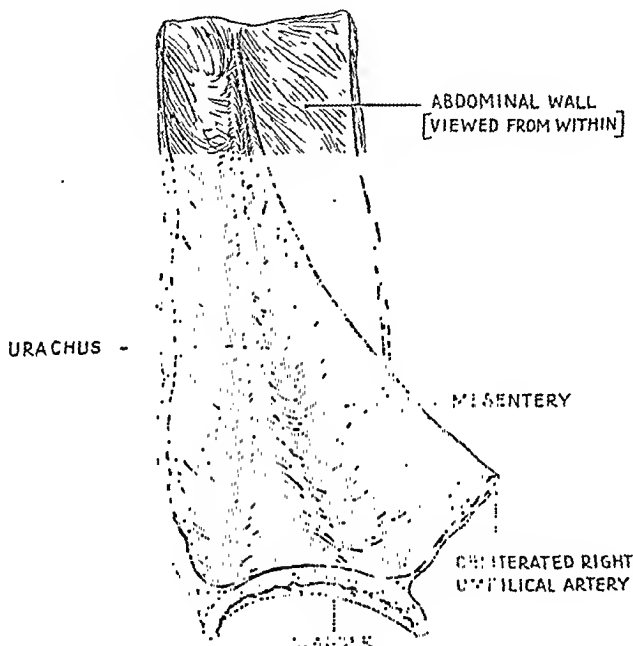


Fig. 1.—Diagrammatic sketch of the umbilical ligament as viewed from within the abdomen.

wall, and along this was a thickened urachus extending from the umbilicus to the vertex of the bladder. The ligament was falciform and was of such breadth that its lower edge almost touched the pelvic floor throughout its length. Along the dorsal border was the thickened, obliterated right umbilical artery, about 0.3 cm. in diameter, attached to the umbilicus at its cephalad end and deep on the right lateral pelvic wall just beyond the distal portion of the hypogastric artery at its caudad. Thus the ligament occupied the midline in its upper portion but swerved to the right in its lower portion. It was in reality a large anomalous ligament formed by fusion of the median and right lateral umbilical ligaments (fig. 1). No left lateral ligament or left umbilical artery was found. The ligament was retracted with some difficulty, and the pelvic organs were exposed. The uterus was a small unicornuate body, firm and cylindric, about 1 cm. in diameter and 3.5 cm. in length. There was no definite demarcation between its fundal and cervical portions. It lay on the pelvic floor, its upper end directed a little to the

left. There was a thin broad ligament on the left, with small uterine vessels. A small round ligament ran from the fundus to the internal inguinal ring. The left tube arose at the cornual end and was 4 or 5 cm. in length; it was normal in appearance, with an open fimbriated end. The left ovary was not remarkable; it measured about 4 by 1 by 1 cm. and occupied a vertical position a little higher than normal along the pelvic wall. Its ligaments were normal. On the right side there was no uterine body and no broad ligament or uterine vessels. The uterine serosa was unattached along its right border and was fused over the cervical portion with the bladder reflection anteriorly and with the pelvic peritoneal wall laterally and posteriorly. The uterus was rotated on its axis to the left, so that the left cornual end was a little posterior and to the right. The only structure

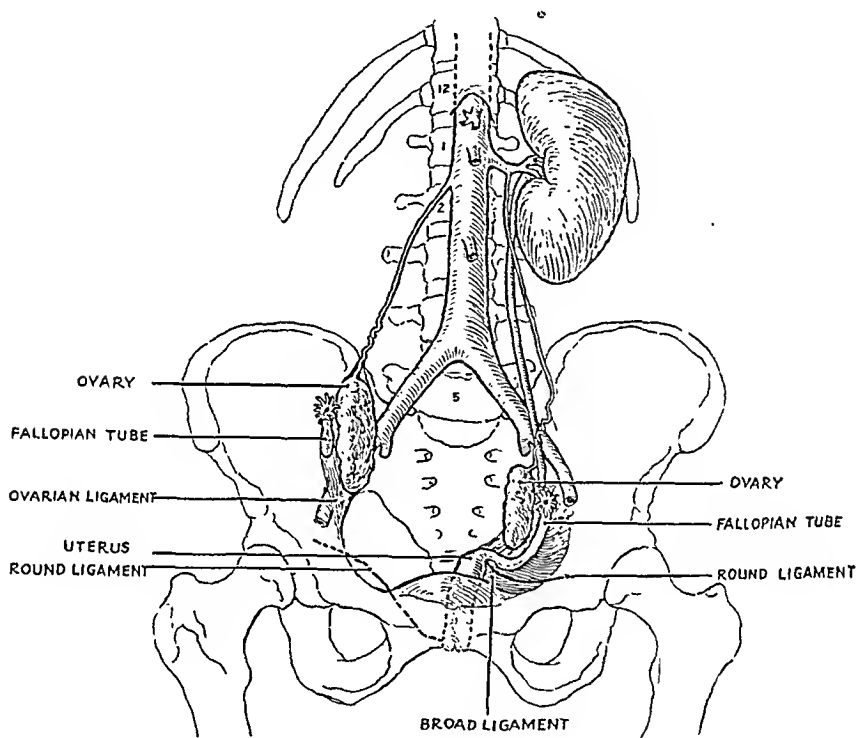


Fig. 2.—Diagrammatic sketch of the urogenital anomaly observed in case 1.

on the right side with any connection with the uterine body was a thin string of muscular tissue which was identified as the round ligament and which passed from the right lateral cervical region across the lower reflection of the bladder along the parietal wall near the insertion of the obliterated umbilical artery and disappeared in the parietal peritoneum near the internal inguinal ring. The right ovary was larger than the left (about 5 by 1.5 by 1.5 cm.) and lay in a vertical position high above the pelvic brim along the inner side of the cecum. Its vessels entered at its upper lateral margin. From the caudad end a thin ovarian ligament extended toward the internal inguinal ring for a distance of from 1.5 to 2 cm., being fused at that point with the parietal peritoneum. Along the lateral border of the ovary, suspended in its own short mesosalpinx, was the fimbriated end of the tube, the remainder being absent. It was about 2 cm. in length, with one end fimbriated and open and the other end closed (fig. 2). No ureter was seen on the

right. There seemed no need for interference with the umbilical ligament. The appendix was amputated in the usual fashion, its stump being inverted with a pursestring suture, and the abdominal wall was closed in layers.

Postoperatively the patient did well. The wound healed per primam. Intravenous pyelograms (16 cc. of diodrast being used) showed a large kidney on the left side (12 by 6 cm.) with normal calices, pelvis and ureter (fig. 3). No renal shadow was seen on the right side in the plain roentgenogram or during excretion of the dye, and no kidney could be palpated on this side. Cystoscopic examination was made with a no. 20 posterior sheath cystoscope, which was easily passed. The bladder was readily visualized. The mucosa appeared normal, and the bladder seemed symmetric. On the left a normal ureteral orifice and ureteral ridge were present, while the interureteral bar, the right ureteral ridge and the orifice were



Fig. 3 (case 1).—Roentgenogram taken five minutes after the injection of 16 cc. of diodrast.

absent. Culture of the urine was sterile. The phenolsulfonphthalein test revealed an excretion of 22 per cent in seven minutes, a total of 57 per cent in one hour and 67 per cent in two hours. The patient, under nitrous oxide anesthesia, was examined by Dr. H. L. Thoms, who found normal external genitalia and a normal small vagina and cervix. The uterocervical canal was measured with a small probe and was found to be 3 to 4 cm. in length. The patient was discharged on March 6.

CASE 2.—Uterus bicornis bicollis; left renal and ureteral agenesis.

C. W., a girl aged 19, had been born and reared in China. The family history was noncontributory. In her second year the patient had an unexplained acute febrile illness. She had had dysentery, measles, mumps, whooping cough and otitis media. The menses began at the age of 11; they were always irregular and rather prolonged and were accompanied by pain, especially on the right side. As early as 1931 she was having a great deal of abdominal pain in addition to the dysmenorrhea, and in 1932 she had a laparotomy performed in Peiping. A

bicornuate uterus was found, and an appendectomy was done. She was examined in August 1936 and was found to have compensated mitral stenosis, chronic nephritis and severe chlorotic anemia. By October she was having a great deal of edema of the ankles. She had had nocturia (two or three times) as long as she could remember. She was admitted to the medical service of the New Haven Hospital in November for diagnostic study and was readmitted in February 1937. She was a short, rather stout girl with a flat nose, a broad face, thick features, short arms and legs and obese buttocks and hips. There was an apical systolic murmur. The right kidney was palpable, but the left was not. Numerous laboratory studies were done. There was microcytic anemia. Examination of the urine revealed albumin, hyaline and granular casts and occasional red cells and leukocytes. The urine was loaded with colon bacilli until three weeks before the patient's discharge on May 29. The nonprotein nitrogen content was normal; the total protein content of the plasma was low (4.1 mg. per hundred cubic centimeters). The phenolsulfonphthalein test revealed a total two hour excretion of 55 per cent but a poor distribution curve during the excretion period. Intravenous pyelograms taken on two occasions showed a large kidney on the right and none on the left. Because of frequent and profuse menses curettage was performed. After a long period of treatment the patient was discharged improved. The diagnosis was congenital aplasia of the left kidney; pyelonephritis of the right kidney; uterus bicornis; endometrial hyperplasia; and dwarfism from an unknown cause, perhaps renal. In June she returned to the gynecologic service because of continued and profuse uterine bleeding. Cystoscopic examination showed normal vesical mucosa, normal capacity, a normal ureteral orifice and ridge on the right side and no ridge or orifice on the left. Because of the continued bleeding it was necessary to do a hysterectomy, particularly in view of the patient's general condition and the inadvisability of her becoming pregnant at any time. At operation a perfectly symmetric uterus bicornis bicollis was found, the two horns being attached in the cervical portion. There was a normal tube and ovary on each side. Supravaginal hysterectomy was done. Convalescence was uneventful.

CASE 3.—*Uterus bicornis unicollis; pyometrium in the right horn with spontaneous uterovaginal fistula; right renal and ureteral agenesis.*

E. B., a girl aged 15, complained of vaginal discharge. The family history was noncontributory, and the patient's history was unimportant except for symptoms referable to the genitourinary system. The menses began at the age of 12 but ceased after two scanty periods. They were reestablished in June 1936, after which they recurred regularly at thirty day intervals, the duration being five days and the flow moderate. There was slight pain during the first two days. In the fall of 1936 she began to have a faint brownish vaginal discharge without any noticeable odor, most marked before and after each period but persisting during the interval. It never required the wearing of a pad.

She dated her present illness back to six months before admission to the hospital, when there was a noticeable increase in the vaginal discharge, which had become bloody or dark brown. For three months there was a foul odor, and for several weeks she had had to wear a pad. For two months there had been occasional enuresis but no other urinary symptoms. For about one week she had complained of rather severe pain in the right lower quadrant of the abdomen. Several days before admission there had been a sudden increase in the vaginal discharge, after which the pain had largely subsided. She was admitted to the hospital on September 18.

General examination disclosed nothing remarkable, and pelvic examination gave no conclusive information except that there was a small vaginal fistulous

opening to the right of the cervix, which had not been found on the patient's previous visits to the dispensary. Just above the sinus tract was a fluctuant, tender swelling, pressure on which caused an evacuation of thick foul-smelling pus through the fistula. The rectal temperature was 99.6 F., and the white blood



Fig. 4 (case 3).—*A*, roentgenogram taken after injection of 15 cc. of skiodan through the vaginal fistula, showing the right uterine horn and tube. *B*, visualization of left uterine horn and tube after injection of iodized poppyseed oil.



Fig. 5 (case 3).—Roentgenogram taken five minutes after injection of 15 cc. of diodrast.

cell count was 13,100. The urine was normal. The nonprotein nitrogen content was 28 mg. per hundred cubic centimeters. The phenolsulfonphthalein test revealed a total excretion of 60 per cent. Culture of the vaginal discharge showed nonhemolytic streptococci, *B. coli* and *Staphylococcus albus*. The sinus tract was probed; a 0.5 ureteral catheter was introduced; 15 cc. of skiodan was

injected, and roentgenograms were taken. Subsequently iodized poppyseed oil was injected through the cervix, and intravenous pyelograms were taken, followed by cystoscopic examination and exploratory laparotomy.

The injection of skiodan through the fistula (fig. 4*A*) outlined the right uterine horn and tube; the intracervical injection of iodized poppyseed oil, the left uterine horn and tube (fig. 4*B*). The pyelograms showed a normal large left kidney but none on the right (fig. 5), and cystoscopic examination revealed absence of the right ureteral orifice and ridge. At laparotomy two separate uterine bodies were seen. That on the right was a little larger than that on the left. Each had a normal-appearing fallopian tube, and there was a normal ovary on either side. The two uterine horns seemed to join in a single cervix. By examination with a speculum it was seen that the cervix was normal in position and appearance. A probe introduced through the cervix passed into the left horn and not into the right, whereas a probe inserted in the fistula passed into the right horn. The final impression was that the patient had uterus bicornis unicollis with stenosis of the right internal os, accumulation of secretions and finally pyometrium in the right horn with rupture into the vagina.

COMMENT

The embryologic development of the female genitourinary system has been carefully worked out, and a complete description may be found in available sources.⁵⁰ Suffice it to say that there is general agreement as to the development and eventual degeneration of the pronephros, the metanephros and the wolffian duct, the origin of the metanephric or renal bud, the formation of the genital fold in which the ovary arises, the development of the müllerian ducts and the fusion of their lower portions to form the uterus. The role of the original mesentery of the mesonephric and genital folds in the formation of the mesosalpinx, the broad ligament and the mesovarium, as well as the role of the inguinal fold in the development of the round ligament, is likewise well known. The debated question as to the dual or single origin of the vagina is of no present concern. The intimate association of the genital and urinary tracts in their embryologic development explains the frequency of concomitant malformation of the two systems. There is general agreement that the true unicornuate uterus represents a real agenesis of the entire müllerian duct (when no fallopian tube is present) or an almost complete agenesis of this structure (when the fimbriated end is present). It is felt that so-called unicornuate uterus with a rudimentary second horn is the result of a different defect.⁵¹ With this anomaly, the müllerian duct

50. (a) Felix: Development of the Urogenital Organs, in Keibel, F., and Mall, F. P.: *Manual of Human Embryology*, Philadelphia, J. B. Lippincott Company, 1912, vol. 2, chap. 19. (b) Koff, A. K.: *Embryology of the Female Generative Tract*, in Curtis, A. H.: *Obstetrics and Gynecology*, Philadelphia, W. B. Saunders Company, 1933, vol. 1, chap. 17.

51. Kermauner, F.: Die Fehler in der Verschmelzung der Müllerschen Gänge. *Ztschr. f. Geburtsh. u. Gynäk.* 72:724, 1912. Felix.^{50a}

apparently develops originally throughout its length, but there is a failure of fusion with the other duct, and varying degrees of maldevelopment occur subsequently. The various types of double uterus are explained on a basis of incomplete fusion. As to the cause of the various genital anomalies, many opinions have been expressed,⁵¹ but these are of necessity only theories.

Of particular interest in my first case was the anomalous umbilical ligament. Such a one as this must be an unusual occurrence, as Cullen⁵² mentioned no case quite like it in his exhaustive treatise. In my experience a similar defect in a young Negro who had no other apparent anomaly has been observed, and several other not dissimilar cases have been found in the literature. Schilling²⁰ presented the case of a 1 day old infant with a left true unicornuate uterus in which the left umbilical artery was entirely absent and the right arose deep along the right pelvic wall, just as it did in my patient. He also noted the lack of one umbilical artery in a fetus with an extremely rudimentary uterus. In a third patient, a 2½ day old baby, there was a left unicornuate uterus and a large and thickened right umbilical artery. He cited Kermauner as having also noted the lack of one umbilical artery, and he pointed out that in this case of unicornuate uterus with a rudimentary horn the lateral umbilical ligament was also anomalous on the side of defective development. Schilling stated that he could draw no conclusions from these observations. It may be postulated that an unusually large umbilical artery or a single umbilical artery may by pressure be a factor in the lack of development of the müllerian duct on that side or in the failure of fusion with the other.

We have shown that genital and renal anomalies frequently occur together; more often in the female than in the male. The genital malformations which are most often associated with renal agenesis are true unicornuate uterus and unicornuate or bicornuate uterus with a rudimentary horn. In addition, however, the various types of symmetric genital anomalies are also not infrequently associated with unilateral agenesis of the kidney. The hazard of the solitary kidney has been repeatedly pointed out.⁵³ It is frequently the site of disease. Nephrolithiasis, ureterolithiasis, nephritis, pyelitis, pyelonephritis, tuberculosis and other disease processes have been frequently found. In too many instances the surgical removal of the single kidney has been followed by disaster. I have pointed out that genital malformations are likewise not without danger. Hematometra and hematosalpinx and pregnancy with rupture in the rudimentary horn occur often in unicornuate or

52. Cullen, T. S.: *Embryology, Anatomy and Diseases of the Umbilicus*, Philadelphia, W. B. Saunders Company, 1916.

53. Campbell.²⁴ Anders.⁴⁴ MacKenzie and Hawthorne.⁴⁵ Gutierrez.⁴⁹

bicornuate uterus with a rudimentary horn. Certain malformations of the internal genitalia require plastic reconstruction. Campbell⁵⁴ has discussed the difficulties met with in the practice of obstetrics. Hence it is essential that every patient with anomalous development of the genital organs be carefully examined from the urologic standpoint and that adequate study of the genital tract be carried out in every instance of congenital renal anomaly. Fortunately, cystoscopic and pyelographic examination will reveal any such defect in the urinary tract. Uterosalphingography is of great assistance in conjunction with the usual gynecologic examination in detecting malformations of the uterus.

SUMMARY

A case of true unicornuate uterus with unilateral renal and ureteral agenesis associated with an anomalous umbilical ligament is presented. A second case of uterus bicornis bicollis with unilateral agenesis of the kidney and ureter is briefly described. A third case of uterus bicornis unicollis with pyometrium in one horn and ureterovaginal fistula and with congenital absence of one kidney and ureter is presented.

The literature is reviewed.

It is pointed out that genital and renal anomalies occur so frequently together as to necessitate careful urologic study in each case of genital malformation and full investigation of the genital organs in each case of renal anomaly.

Drs. John P. Peters, Clarence L. Robbins and Herbert Thoms and Drs. Arthur H. Morse and Ralph H. Jenkins gave me permission to report their cases.

The illustrations were drawn by Mr. Arnim Hemberger.

54. Campbell, A. M.: Disturbances Due to Diseases and Abnormalities of the Female Genitalia, in Curtis, A. H.: *Obstetrics and Gynecology*, Philadelphia, W. B. Saunders Company, 1933, vol. 2, chap. 31.

CONCENTRATION OF PROCAINE IN THE CEREBRO- SPINAL FLUID OF THE HUMAN BEING AFTER SUBARACHNOID INJECTION

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From the introduction of spinal anesthesia (in 1899) to the present time speculation has been almost continuously rife concerning the behavior of the anesthetic after injection. Although the suggestion was made as early as 1901 by J. S. Miller¹ that it would be important to study the actual concentration of the anesthetic in the cerebrospinal fluid, most attempts to solve the problem have been based on studies of the behavior of fluids injected into inanimate models, into cadavers and occasionally into experimental animals. On the basis of such studies and on a priori reasoning of doubtful validity these authors have concluded that anesthetic solutions of greater density than the cerebrospinal fluid flow downward toward the head if the patient is immediately placed in the Trendelenburg position.

In a recent paper² this point of view has been adopted again, and various measures have been indicated to prevent untoward results from the high concentration of procaine which it was assumed might reach the medullary centers under these conditions. Since this report and those which preceded it contained no direct evidence, and since we had already obtained data which indicated by inference that procaine solutions injected into the subarachnoid space of the human being behave differently from the same solutions similarly injected in inanimate models, further studies were made on the concentration of procaine in the cerebrospinal fluid during spinal anesthesia.

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1. Miller, J. S.: The Present Status of the Subarachnoidian Injection of Cocaine for Anesthesia (Corning-Bier Method), New York M. News **78**:375-377, 1901.

2. Pratt, G. H.: The Safety Factor in Spinal Anesthesia, Surg., Gynec. & Obst. **64**:695-699, 1937.

In a preliminary paper³ we reported on the concentration of procaine in the subarachnoid space at the site of injection at various intervals during the course of spinal anesthesia. In this paper we are presenting data obtained in a similar manner on the concentration of procaine in the spinal fluid three interspaces above the site of injection and on its concentration in the cisterna magna.

METHOD

One hundred and twenty-two adult patients were studied. Each patient received an injection of 150 mg. of procaine hydrochloride dissolved in 3.5 cc. of cerebrospinal fluid at the interspace between the second and the third lumbar vertebra. The injected solution had a specific gravity of 1.0097, as compared with 1.0015 for the spinal fluid alone. The patients were then placed in a modified Trendelenburg position, at angles of 5 to 8 degrees.

At different intervals after the injection samples of cerebrospinal fluid were withdrawn from various patients. From one group, of 40 patients, samples of

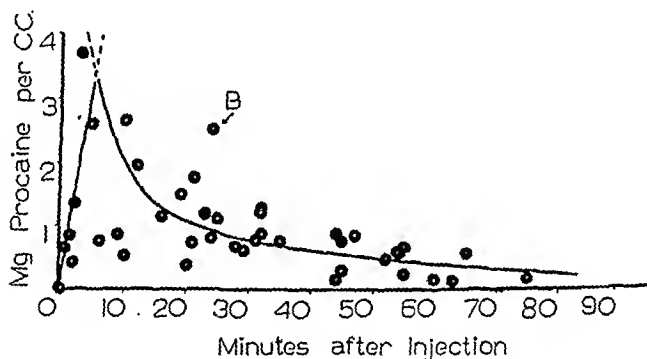


Chart 1.—Concentration of procaine in the cerebrospinal fluid three interspaces above the site of injection in different patients at various intervals after the injection of the anesthetic.

1 cc. were withdrawn three interspaces above the site of injection. From another group, of 22 patients, samples of about 2 cc. were withdrawn from the cisterna magna. The concentration of procaine in these samples was determined, in most cases in duplicate or in triplicate, by the micromethod previously described,⁴ with an error not over 10 per cent.

RESULTS

The concentrations of procaine in the spinal fluid three interspaces above the site of injection are shown graphically in chart 1. The corresponding data on the concentration of the anesthetic at site of injection are shown, for comparison, in chart 2.

3. Koster, H.; Shapiro, A., and Leikensohn, A.: Procain Concentration Changes at Site of Injection in Subarachnoid Anesthesia, *Am. J. Surg.* **33**:245-248, 1936.

4. Koster, H.; Shapiro, A., and Posen, E.: A Micromethod for the Quantitative Determination of Procain in Cerebro-Spinal Fluid, *J. Lab. & Clin. Med.* **21**: 1096-1098, 1936.

At the moment of injection of the anesthetic its concentration in the spinal fluid three interspaces above is zero. Chart 1 shows that it rises rapidly in the first four minutes to a concentration just below 4 mg. per cubic centimeter. At this time the concentration is already approximately the same as at the site of injection. From this time on, the concentrations three interspaces above and at the site of injection decrease at approximately the same rate.

At no time does the concentration at the dorsal level rise above that at the lumbar level, despite the use of the Trendelenburg posture and of a solution with a density higher than that of the cerebrospinal fluid.

Chart 3 shows the concentrations of procaine found in the cisternal fluid at various intervals after injection. In 14 instances almost no

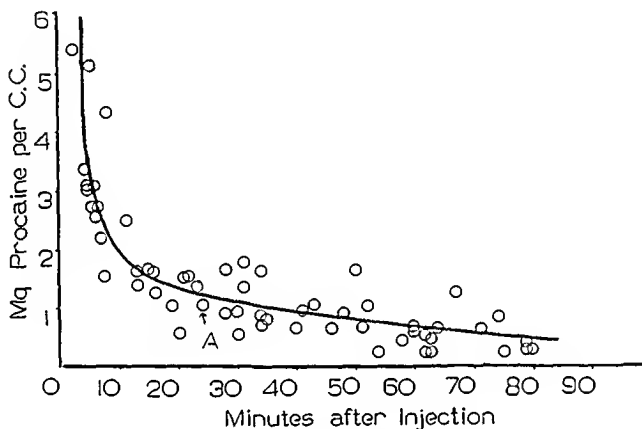


Chart 2.—Concentration of procaine in the cerebrospinal fluid at the site of injection in different patients at various intervals after the injection of the anesthetic.

procaine was found (less than 0.02 mg. per cubic centimeter). In the other 8 instances the concentration ranged from 0.06 to 0.21 mg. per cubic centimeter.

COMMENT

Many authors (Pratt,² Pitkin,⁵ Co Tui,⁶ Vehrs⁷ and Babcock⁸), having observed phenomena obtained by injection of colored fluids

5. Pitkin, G. H.: Controllable Spinal Anesthesia, *Am. J. Surg.* **5**:537-553, 1928.

6. Co Tui, F. W.: Further Studies in Subarachnoid Anesthesia, *Anesth. & Analg.* **13**:143, 1934.

7. Vehrs, A. R.: Problems in the Hydrodynamics of Analgesics in the Subarachnoid Fluid of Man: Diazotized Novocaine in Artificial Dural Sacs, *West. J. Surg.* **43**:16-32, 1935.

8. Babcock, W. W.: Spinal Anesthesia in Fact and Fancy, *Surg., Gynec. & Obst.* **59**:94-100, 1934.

into artificial cerebrospinal systems made of glass tubes, have concluded by analogy that anesthetic solutions of greater density than cerebrospinal fluid settle in dependent portions of the subarachnoid space shortly after injection. On this basis they have devised elaborate systems for controlling anesthesia levels by manipulating the position of the patient, without, however, providing any adequate statistical evidence for the validity of their assumptions.

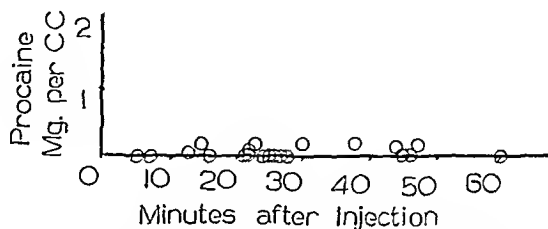


Chart 3.—Concentration of procaine in the cerebrospinal fluid in the cisterna magna in different patients at various intervals after the injection of the anesthetic.

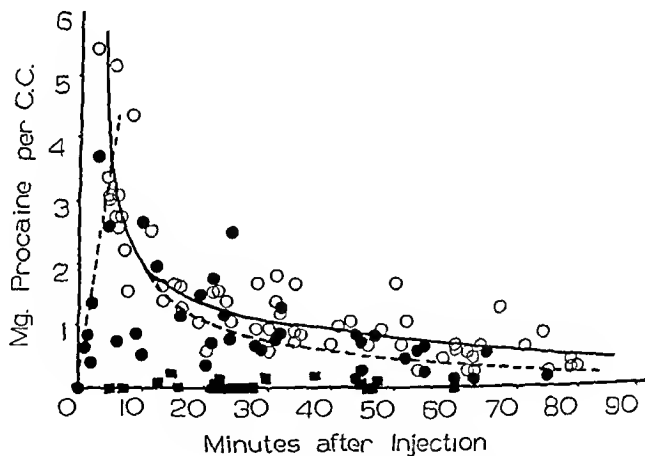


Chart 4.—Composite plot of concentrations of procaine in samples of spinal fluid obtained at various levels: at the site of injection (open circles, solid line), three interspaces above (solid circles, broken line) and at the cisterna magna (solid squares).

Inspection of charts 1 and 2 indicates a considerable range of variation among different patients. For example, the patient represented by point *A* in chart 2 showed a concentration of 1.05 mg. per cubic centimeter at the site of injection after twenty-five minutes. Another patient, represented by point *B* in chart 1, had a concentration of 2.5 mg. per cubic centimeter three interspaces above the site of injection

after twenty-four minutes. If one were to consider only these two observations, made at approximately the same interval after the injection of the anesthetic, one would conclude that because of the Trendelenburg position the concentration in the dorsal region was twice that in the lumbar region and that it indicated a gravitational displacement from the site of injection toward the head. On the same basis one might also expect an even higher concentration further cephalad.

However, an examination of all the data indicates that conclusions drawn from these two observations alone would be wholly erroneous. On the contrary, the average concentration is never greater in the dorsal region than in the lumbar region, and the concentration in the cisterna magna is always considerably lower than at either of the other sites investigated.

To show more clearly the simultaneous values for the concentration of procaine at the three levels investigated, all of the determinations have been plotted on the same axes in chart 4. This chart clearly demonstrates the essential phenomena of the distribution of procaine in the subarachnoid space of the patient during spinal anesthesia. The injected procaine spreads rapidly away from the site of injection, so that in the first few minutes the concentration decreases rapidly there while it is rising at the dorsal level. When the concentration at the dorsal level has reached its maximum, it decreases at a rate approximately the same as that at the lumbar level, and presumably for the same reasons.

The maximum concentration at the site of injection is that of the injected solution (43 mg. per cubic centimeter) at the moment of injection. The maximum concentration only three interspaces above is never above 4 mg. per cubic centimeter and is reached in four minutes. This great decrease is continued in the cephalad direction, so that the cisternal values are never greater than 0.21 mg. and are frequently less than 0.02 mg. per cubic centimeter.

In other words, our observations indicate definitely that in the living human patient the Trendelenburg posture does not cause a procaine solution of greater density than cerebrospinal fluid to flow downward toward the head.

SUMMARY

With 122 patients anesthetized by the injection of 150 mg. of procaine hydrochloride into the subarachnoid space, the concentration of the anesthetic was determined at various intervals after the injection: (1) in 60 patients, at the site of injection; (2) in 40 patients, three interspaces above the site of injection, and (3) in 22 patients, in the cisterna magna. The data indicate that the injected anesthetic is distributed rapidly cephalad. The peak concentration reached at a particular level

during anesthesia decreases rapidly in the cephalad direction, so that in the cisterna magna the concentration of procaine was never above 0.21 mg. per cubic centimeter, and in 14 of 22 samples it was less than 0.02 mg.

These findings do not support the assumption that the Trendelenburg position causes concentrated solutions of procaine to flow down to the cisterna as do colored solutions in inanimate models.

EFFECT OF BILIARY OPERATIONS ON THE LIVER

THEIR RELATION TO THE CONCENTRATION OF BILE ACIDS IN BILE

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It has been shown previously that a liver injured by biliary disease is unable to concentrate bile acids in bile. Two of us in association with Nettrour and Bollman¹ have demonstrated that the loss of this function parallels the degree of hepatic injury. While a normal liver was found to concentrate from 2,000 to 3,000 mg. of bile acids in each hundred cubic centimeters of bile, a severely injured liver did not concentrate more than 500 mg.

It was noted also that an inhibition in the concentration of bile acids by the liver followed operations on the biliary tract. The concentration of bile acids decreased progressively until the third or fourth day after operation and then gradually returned, reaching the same concentration on the ninth day as had existed immediately after operation. This was taken to represent the time at which the liver had completely recovered from the temporary inhibition of function resulting from conditions associated with the surgical procedure. After a variable period there was a further increase in the concentration of bile acids in the bile, and a plateau was reached between the second week and the third month after operation. We expressed the opinion that this represented the recovery of the liver from temporary injury resulting from the biliary disease that existed before operation. The final plateau reached was below the normal level in all cases in which there was clinical and pathologic evidence of permanent injury of the liver.

This report deals with the results of the study of the effect of operation on the liver. The influence of the length of the operative procedure,

From the Division of Surgery, the Mayo Clinic.

1. Gray, H. K.; McGowan, J. M.; Nettrour, W. S., and Bollman, J. L.: Hepatic Damage in Biliary Disease: Its Relation to the Concentration of Bile Acids in the Bile, Arch. Surg., to be published.

of the choice of the anesthetic agent, of the drugs used in postoperative care, of the postoperative febrile reaction and of the clamping off of the T tube were estimated. As an indicator of the effect on the liver, the concentration of bile acids in bile was used. Daily and at times hourly samples of bile were collected from patients into whose common bile duct a T tube had been inserted for prolonged biliary drainage.

Bollman, Mann, and one of us,² who corroborated the work of McMaster, Broun, and Rous,³ observed a decrease in the concentration of bile acids in the bile of 11 dogs which had normal livers after the removal of the gallbladder and the placing of a cannula in the common bile duct during ether anesthesia. There was a decrease also in the total amount of bile acids excreted in the bile, and none appeared in the blood or in the urine. In other words, the liver had partly lost its ability to produce and to concentrate bile acids. The total output of bile acids rose to above normal on the fourth postoperative day and then settled down to a constant level on the sixth postoperative day.

In the work which we are reporting we have attempted to find out whether any factors related to the surgical procedure were responsible for the postoperative inhibition of hepatic function and whether there was any fluctuation in the concentration of bile acids from one time of the day to another.

Josephson and Larsson,⁴ Forsgren,⁵ and Trémolières and his associates⁶ claimed that there was a periodic variation in the flow of bile in six hours. Wisner and Whipple,⁷ on the other hand, failed to find any difference in the flow of bile during the day and during the night.

We attempted also to find reasons for incidental decreases in the concentration of bile acids during convalescence in order to determine whether complications of the condition or drugs given for relief of symptoms injured the liver.

2. McGowan, J. M.; Bollman, J. L., and Mann, F. C.: The Bile Acids in Icterus Produced by Toluylenediamine, *J. Pharmacol. & Exper. Therap.* **58**:305-311 (Nov.) 1936.

3. McMaster, P. D.; Broun, G. O., and Rous, P.: Studies of the Total Bile: I. The Effects of Operation, Exercise, Hot Weather, Relief of Obstruction, Intercurrent Disease, and Other Normal and Pathological Influences, *J. Exper. Med.* **37**:395-420 (March) 1923.

4. Josephson, B., and Larsson, H.: Ueber die Periodizität der Gallensekretion bei einem Patienten mit Gallenfistel, *Skandinav. Arch. f. Physiol.* **69**:227-236, 1934.

5. Forsgren, E., cited by Josephson and Larsson.⁴

6. Trémolières, F.; Thiéry, J. É., and Fauchet, H.: Étude d'une fistule biliaire chez l'homme, *Rev. de méd., Paris* **50**:509-531 (Oct.) 1933.

7. Wisner, F. P., and Whipple, G. H.: Variations in Output of Bile Salts and Pigments During Twenty-Four Hour Periods: Observations on Standard Bile Fistula Dogs, *Am. J. Physiol.* **60**:119-133 (March) 1922.

Bollman and Mann⁸ and Smyth and Whipple⁹ have shown that small doses of hepatotoxins, that is, chloroform, carbon tetrachloride and tetrachlorethane, produced a definite decrease in the concentration of bile acids in the bile.

POSTOPERATIVE DROP IN THE VALUES OF BILE ACIDS IN BILE

All the patients exhibited a distinct drop in the level of the bile acids after the operation. This drop was pronounced and was present immediately after operation; it often reached its maximum on the third postoperative day. The possible effect of anesthesia, the operative procedure and the postoperative measures generally employed were studied.

EFFECT OF ANESTHETIC AGENTS

Ether, cyclopropane and ethylene were used alone and in combination. In addition, spinal anesthesia and regional abdominal block with procaine hydrochloride were used alone and in combination with one of these gases.

For the sake of brevity, a few cases in which the quantitative determinations of bile acids were made on the third and the fifteenth postoperative day are listed, in order to give an impression of the extent of the postoperative drop. By the fifteenth day the recovery from the postoperative drop should be complete, although the value for the concentration of bile acids may not return to normal until much later. The reason for this is that in cases in which there is a considerable amount of hepatic injury before operation the regeneration of the liver after surgical relief of biliary obstruction must of necessity be slow.

In order to control the comparison of the anesthetic agents as well as possible, the cases were classified as to the amount of preoperative injury of the liver according to the standards used in a previous communication.¹ A group of cases in which the liver was approximately normal was chosen for study of the effect of the anesthetic (table 1).

It is evident that the choice of the anesthetic agent does not determine to any marked degree the extent of the postoperative decrease in the concentration of bile acids. The number of cases is small for the drawing of definite conclusions. There is, however, a suggestion that the concentration of bile acids was low when ethylene was employed as one of the anesthetic agents. This is reminiscent of the illness which followed hepatic injury among workers in airplane factories who were

8. Bollman, J. L., and Mann, F. C.: The Influence of the Liver in the Formation and Destruction of Bile Salts, *Am. J. Physiol.* **116**:214-224 (June) 1936.

9. Smyth, F. S., and Whipple, G. H.: Bile Salt Metabolism: I. Influence of Chloroform and Phosphorus on Bile Fistula Dogs, *J. Biol. Chem.* **59**:623-636 (April) 1924.

using trichlorethylene in the treatment of the fabric for airplane wings during the World War.

EFFECT OF THE OPERATIVE PROCEDURES

The operative procedures did not vary widely. They consisted of cholecystectomy and choledochostomy, hepaticostomy and reconstruction of the common bile duct over a T tube. Because the procedures

TABLE 1.—*Effect of Anesthesia on Concentration of Bile Acids in Cases in Which the Liver Was Normal Before Operation*

Case	Anesthetic Agent	Concentration of Bile Acids (Mg. per 100 Cc. of Bile)	
		Third Day After Operation	Fifteenth Day After Operation
1	Cyclopropane.....	845	1,880
2	Cyclopropane.....	1,070
3	Cyclopropane; ¾ ounce (22.18 cc.) of ether.....	630	1,950
4	Cyclopropane; 1 ounce (29.57 cc.) of ether.....	1,570*	2,590
5	Cyclopropane; ¾ ounce (22.18 cc.) of ether.....	823	1,830
6	Cyclopropane; ether.....	1,050	1,520
7	Cyclopropane; 1 ounce (29.57 cc.) of ether.....	910*
8	Ethylene; 2 ounces (59.15 cc.) of ether.....	410	2,590
9	Ethylene; 1½ ounces (44.36 cc.) of ether; spinal anesthesia.	435	1,809
10	Ethylene; ½ ounce (14.79 cc.) of ether.....	754	1,430
11	Spinal anesthesia.....	1,350	2,440

* Determination made on fifth day after operation.

TABLE 2.—*Effect of Cholecystectomy and Choledochostomy on Concentration of Bile Acids in Cases in Which the Liver Was Normal Before Operation*

Case	Length of Operation		Concentration of Bile Acids (Mg. per 100 Cc. of Bile)	
	Hours	Minutes	Third Day After Operation	Fifteenth Day After Operation
1	..	55	1,570	2,590
2	..	50	630	1,950
3	1	30	823	1,830
4	1	45	845	1,880
5	2	..	1,050	1,520
6	2	..	2,200

were all limited to the biliary tract, the cases listed in table 2 have been classified particularly as to the length of time involved in the operation, in order to determine whether or not there was an influence on the postoperative decrease in the concentration of bile acids. Cyclopropane anesthesia was used in all the cases, and the livers were classified as approximately normal before operation. Apparently, neither the type nor the length of the operative procedure makes any difference in the postoperative decrease in the concentration of bile acids.

RETURN OF THE CONCENTRATION OF BILE ACIDS TO NORMAL

The depression in the concentration of bile acids which occurs after operations on the biliary tract is followed by an increase. The rate at which this increase occurs varies in different cases. A comparison of the postoperative course and the rate of recovery of the ability of the liver to concentrate bile acids revealed one fact, namely, that the increase in the concentration of bile acids is slow until the postoperative febrile

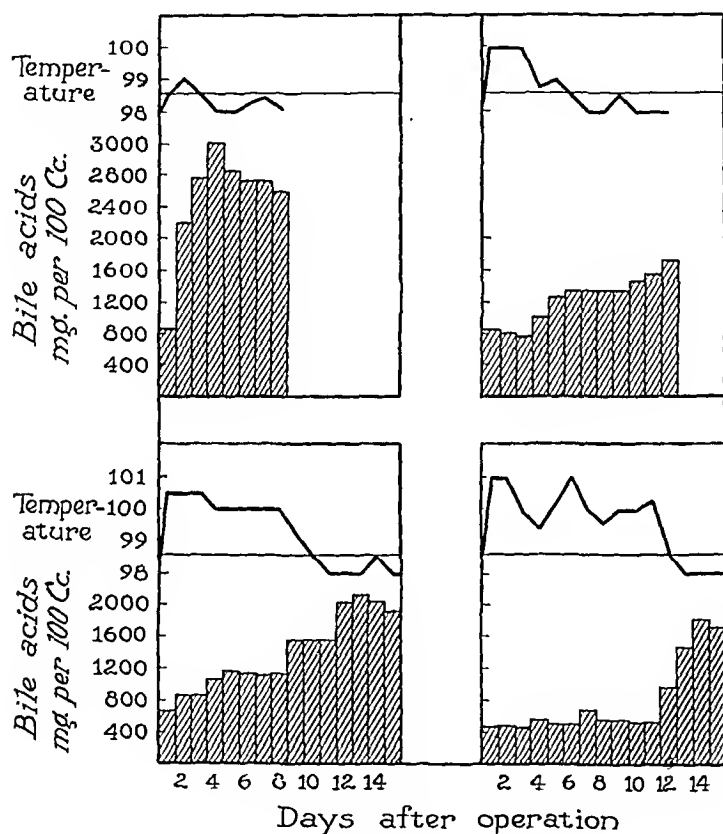


Chart 1.—Relation of the postoperative concentration of bile acids to the febrile reaction.

reaction has ceased. Thereafter the increase is rapid and complete (chart 1). In the case represented in the upper left part of chart 1 there was no febrile reaction, and the increase in the concentration of bile acids began on the second day after the operation.

By contrast, in the case represented in the lower right part of chart 1 the postoperative fever did not abate until the twelfth day, at which time the concentration of bile acids began to rise sharply. In the other cases represented in the chart there were varying degrees of prolongation both

of the febrile reaction and of the recovery of the normal concentration of bile acids. In all the cases represented in this chart cholecystectomy and choledochostomy were performed; jaundice was not present before operation.

EFFECT OF POSTOPERATIVE MEASURES

Sedative Drugs.—In order to determine whether the use of derivatives of opium and barbiturates played any role in delaying the return of the concentration of bile acids to normal, the value for the concentration of bile acids was determined at intervals of two hours for several

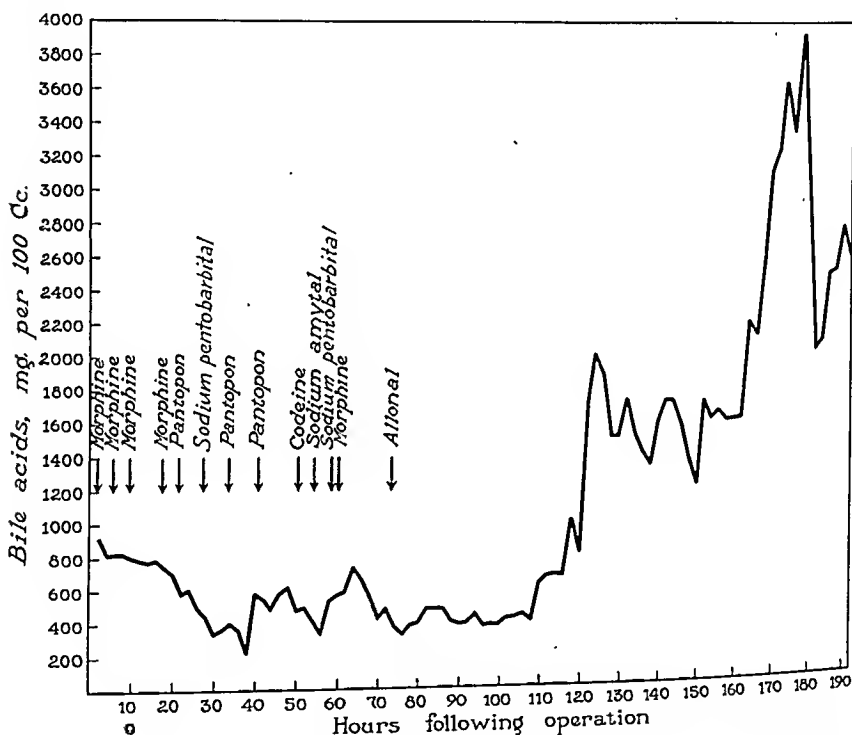


Chart 2.—Effect of sedative drugs on the concentration of bile acids after operation.

days after the operation. The exact time at which the sedatives were given was determined and was compared with the concentration at that time. The curve in chart 2 represents the return of the concentration of bile acids to normal in a case in which cholecystectomy and choledochostomy were performed. As may be seen, there was no relation between the concentration of the bile acids and the administration of morphine, pantopon (a mixture of the hydrochloride of the opium alkaloids), codeine, sodium pentobarbital or sodium amytal. In 2 other cases in which these observations were repeated similar results were obtained.

Intravenous Administration of Dextrose.—Because intravenous administration of dextrose has been of much value in the treatment of hepatic disease, the value for the concentration of bile acids was determined in cases in which dextrose was used. A case of stricture of the common bile duct and deep jaundice relieved surgically by reconstruction of the common bile duct over a T tube was selected. The concentration of bile acids was determined at intervals of two hours, the first determination being made immediately after operation. The times at which dextrose was administered intravenously were plotted on the curve which represented the return of the concentration of bile acids to normal after operation (chart 3). From observation of this curve it

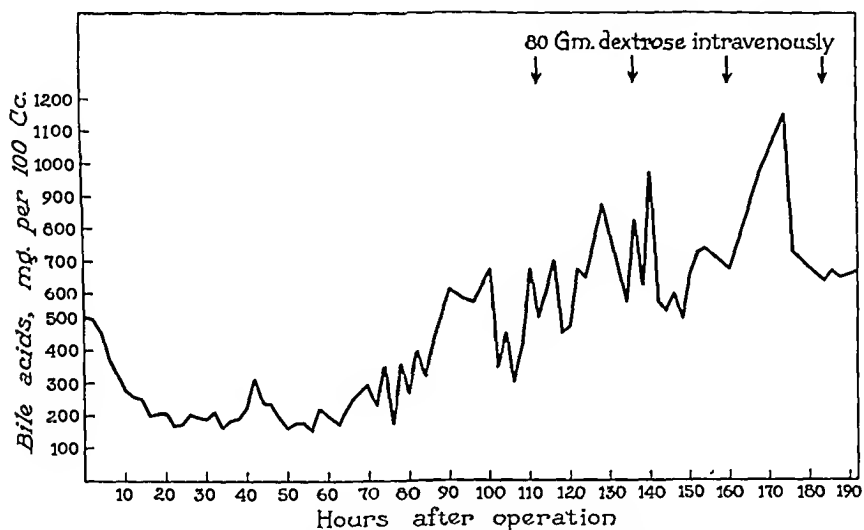


Chart 3.—Effect of intravenous administration of dextrose on the postoperative concentration of bile acids.

may be said that the intravenous administration of dextrose has no immediate effect on the concentration of bile acids. In 2 cases in which these observations were repeated the results were the same.

As an additional check, the concentration of bile acids was determined at intervals of thirty minutes after the intravenous injection of 1,200 cc. of a 10 per cent solution of dextrose. There was no appreciable change in the concentration of bile acids beyond that which might be expected as a result of the dilution produced by the administration of 1,200 cc. of fluid. The results in this case, in which the liver had been injured by prolonged obstruction by a stone in the common bile duct, are shown in chart 4.

EFFECT ON THE CONCENTRATION OF BILE ACID
PRODUCED BY CLAMPING OF THE T TUBE

In cases in which there was a free flow of bile into the duodenum, the values for the concentration of bile acids continued to increase during the gradually increasing periods each day in which the T tube was clamped off. This was further evidence that a free passageway for the bile actually did exist. Had there been any obstruction to the passage of the bile the resultant damming back of the bile in the liver would have resulted in a diminished concentration of bile acids similar to that observed after obstruction of the common bile duct by stones. One case in particular is deserving of more detailed description:

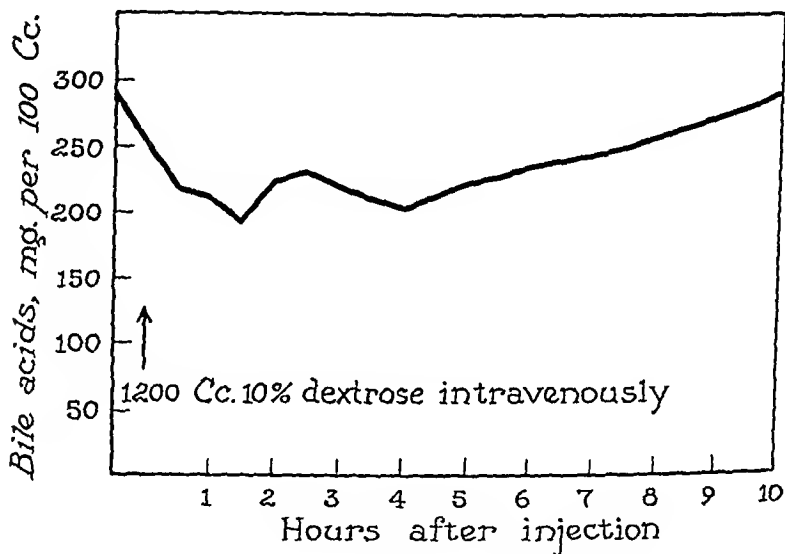


Chart 4.—Behavior of bile acids after intravenous injection of dextrose.

REPORT OF A CASE

The patient complained of continued colic following cholecystectomy. Exploratory laparotomy revealed apparent spasticity of the sphincter of Oddi; there was no organic obstruction of the common bile duct. When the clamping of the T tube was begun, on the twenty-eighth postoperative day, the patient had cramps in the right upper quadrant of the abdomen. Simultaneously the concentration of bile acids dropped from 3,120 mg. to 1,390 mg. for each hundred cubic centimeters of bile. Because of this, no further attempts were made to clamp the T tube. From the thirtieth to the fifty-seventh postoperative day the concentration of bile acids varied from 1,600 to 2,200 mg. per hundred cubic centimeters. On the fifty-seventh postoperative day the clamping of the T tube was again begun, and glyceryl trinitrate was given simultaneously three or four times a day to relieve the cramping sensations. When the spastic obstruction of the common bile duct had been relieved with glyceryl trinitrate, the values for the concentration of bile acids rose to 3,500 mg., and remained at from 3,000 to 3,600 mg. per hundred cubic centimeters.

This brings up the conception of the value of determining the concentration of bile acids before deciding to remove the T tube. Walters and Thiessen¹⁰ have demonstrated the use of postoperative choledochographic study in determining the patency of the common bile duct. Walters and two of us¹¹ have shown the importance of making certain by means of a manometer that there is no increased pressure within the common bile duct before removing the T tube. By both procedures the physician may learn the status of the common bile duct at a given time. The determination of the concentration of bile acids in a twenty-four hour sample of bile furnishes an estimate of the patency of the common bile duct for twenty-four hours. For example, in the case cited, the opaque medium was seen roentgenographically to pass into the duodenum, but the clamping of the T tube caused a diminution in the concentration of bile acids. This was probably caused by spasticity of the sphincter of Oddi, which intermittently obstructed the common bile duct and prevented the flow of bile into the duodenum.

In many cases in which there has been long-continued obstruction of the common bile duct by a stone and resultant severe hepatitis the surgeon determines at the operating table that biliary drainage for from three months to a year is needed in order that cholangitis and hydrohepatosis may have time to subside. Later determinations of the concentration of bile acids before the T tube is removed will serve to reenforce his judgment as to how long the T tube should be allowed to remain in place.

COMMENT

A decrease in the concentration of bile acids in bile was demonstrated after operations on the biliary tract in all cases studied. This evidence of inhibition of hepatic function assumes grave significance when one is called to operate on a patient who already has suffered severe hepatic injury as a result of prolonged obstruction of the biliary tract. Therefore, one should exercise every known method to improve hepatic function if possible before operation. Therapeutic measures which would prevent the postoperative decrease in the concentration of bile acids would be ideal. More work needs to be done to find some protective hepatic substance which will do this. We feel that the determination of the concentration of bile acids in the bile is an excellent indicator of the usefulness of new methods for improving the function of the liver before operation and thereby reducing the operative risk.

10. Walters, W., and Thiessen, N. W.: Visual Methods of Studying the Physiology of the Common Bile Duct: I. The Problem of Pancreatitis and Sphincteritis, *Proc. Staff Meet., Mayo Clin.* 9:772-775 (Dec. 19) 1934.

11. Butsch, W. L.; McGowan, J. M., and Walters, W.: Clinical Studies on the Influence of Certain Drugs in Relation to Biliary Pain and to the Variations in Intrabiliary Pressure, *Surg., Gynec. & Obst.* 63:451-456 (Oct.) 1936.

The degree and duration of the postoperative febrile reaction is paralleled by an inhibition of the ability of the liver to concentrate bile acids. From this one may deduce that a patient who has a severely injured liver will be handicapped in dealing with an infective process accompanied by a febrile reaction, particularly when this is added to the extra injury which the liver suffers during the operation.

The clamping of the T tube in the presence of obstruction to the free flow of bile into the duodenum has been followed by a progressive reduction of the concentration of bile acids in the bile. This is a result of increased pressure within the common bile duct, one of the factors that produce the hepatic injury before operation in cases of obstruction of the biliary tract. Counseller and McIndoe¹² have shown that in the presence of biliary obstruction there is a marked dilatation of the finer radicles of the biliary tree (hydrohepatosis). Such dilatation may result in pressure on the parenchymal cells of the liver, which produces atrophy.

It might be argued that the decrease in the concentration of bile acids after the clamping of the T tube was due to the choleretic effect of the extra amounts of bile acids which are absorbed from the intestinal canal. However, in the cases in which there was every evidence of patency of the lower end of the common duct there was no appreciable diminution of the concentration of bile acids in the bile after the clamping of the T tube.

SUMMARY

Repeated specimens of bile were analyzed postoperatively in cases in which operation was done, in order to measure, by the concentration of bile acids in the bile, the effect of various surgical procedures on the functions of the liver. A postoperative inhibition of hepatic function occurred in every case. This seemed to be unassociated with the duration of the surgical procedure, with the type of anesthetic (with the possible exception of ethylene) and with the preoperative and postoperative medication. The usual postoperative doses of morphine and barbiturates failed to produce any effect on the concentration of bile acids.

The duration and degree of the postoperative febrile reaction paralleled the duration of the inhibition of hepatic function. When the T tube was clamped in the presence of obstruction to the free flow of bile into the duodenum, the concentration of bile acids decreased progressively.

12. Counseller, V. S., and McIndoe, A. H.: The Dilatation of the Bile Ducts (Hydrohepatosis), *Surg., Gynec. & Obst.* 43:729-740 (Dec.) 1926.

SUBACROMIAL BURSITIS

A CLINICAL, ROENTGENOGRAPHIC AND STATISTICAL STUDY

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Credit is generally given to Codman¹ for centering attention on and stimulating interest in the proper diagnosis and treatment of complaints referable to the region around the shoulder joint. As a result of a series of articles on the subject which he began in 1904 and culminated in his book on the shoulder in 1934, Codman has developed the clinical syndrome of subacromial bursitis and has given physicians a greater understanding of the differential diagnosis of the extra-articular lesion of the shoulder. He gave due credit to previous workers, including Duplay,² Putman,³ Monks⁴ and Küster,⁵ for their contributions to the subject. He credited the monograph of Duplay with representing the

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Abstract of a thesis submitted to the faculty of the Graduate School of the State University of Iowa in partial fulfilment of the requirements for the degree of Master of Science in Orthopedic Surgery. The work was done in the service of Dr. Arthur Steindler.

1. (a) Codman, E. A.: Some Points on the Diagnosis and Treatment of Certain Neglected Minor Surgical Lesions, Boston M. & S. J. **150**:371-375, 1904; (b) On Stiff and Painful Shoulders: The Anatomy of the Subdeltoid or Subacromial Bursa and Its Clinical Importance; Subdeltoid Bursitis, *ibid.* **154**:613-620, 1906; (c) Bursitis Subacromialis, or Periarthritis of the Shoulder Joint, *ibid.* **159**:533-537, 576-582, 615-616, 644-648, 677-681, 723-726 and 756-789, 1908; (d) Complete Rupture of the Supraspinatus Tendon: Operative Treatment with Report of Two Successful Cases, *ibid.* **164**:708-710, 1911; (e) On Stiff and Painful Shoulders as Explained by Subacromial Bursitis and Partial Rupture of the Supraspinatus, *ibid.* **165**:115-120, 1911; (f) The Shoulder, Boston, The Author, 1934. (g) Codman, E. A., and Akerson, I. B.: The Pathology Associated with Rupture of the Supraspinatus Tendon, *Ann. Surg.* **93**:348-359, 1931.

2. Duplay, S.: De la périarthrite scapulo-humérale et des raideurs de l'épaule qui en sont la conséquence, *Arch. gén. de méd.* **2**:513-542, 1872.

3. Putman, I. I.: The Treatment of a Form of Painful Periarthritis of the Shoulder, Boston M. & S. J. **107**:509-538, 1882.

4. Monks, G. H.: A New Method for the Treatment of Injuries to the Shoulder, Boston M. & S. J. **123**:183, 1890.

5. Küster, E.: Ueber Bursitis subacromialis (Periarthritis humero-scapularis), *Verhandl. d. deutsch. Gesellsch. f. Chir.* **31**:364-372, 1902.

knowledge previous to the publication of Küster's article and the latter author with opening a new era in the consideration of these lesions.

The purpose of this paper is to present a clinical, roentgenographic and statistical study of subacromial bursitis and to review the experience in 288 cases in which the condition was treated in the clinic of Dr. Arthur Steindler, in the department of orthopedic surgery at the State University of Iowa.

ANATOMIC PICTURE

The subacromial bursa intervenes between the deltoid muscle and the acromion externally and the capsule and the short rotators of the shoulder joint internally. Interposed thus between the acromial arch and the lateral surface of the shoulder joint, it is indispensable in abduction and rotation and allows for abduction of the humerus without pinching of the deltoid fibers. In right angle abduction, the entire bursa may lie under the acromion. The subacromial and subdeltoid portions may be separated by a thin fibrous partition. However, these divisions of the bursa form one large cavity and should be considered as one large bursal sac, especially as the dividing partition is usually absent. A proper understanding of the subject can be had only by considering the bursa in its entirety rather than in parts. The term subacromial bursitis will be used throughout this paper rather than subdeltoid bursitis, as it is more descriptive of the lesion.

The size of the bursa is variable. It has been described as being as large as the palm of the hand. Filling the bursa with solids for purposes of measurement, as done by Turner Thomas,⁸ causes an increase of the thickness with a corresponding decrease in the diameter; this results in incorrect determination. The size of the bursa cannot be estimated from calcification as it appears in roentgenograms. The areas of calcification are usually outside the bursa. If within the bursa, they rarely if ever completely fill the bursal sac.

In the erect position, abduction of the arm is initiated by the supraspinatus muscle. When motion at the shoulder is limited, movement is continued by motion of the scapula. The mechanical difficulties involved in maintaining the stability of the shoulder joint, with their resultant strain on the tendons inserting into the capsule, are an important factor in producing ruptures of these tendons, with secondary involvement of the intimately associated subacromial bursa.

6 and 7. Footnotes deleted.

8. Thomas, T. T.: Stiff and Painful Shoulders with Loss of Power in the Upper Extremity, *Am. J. M. Sc.* **141**:515-534, 1911.

ETIOLOGY

Pathologic conditions of the bursa may result from (1) local trauma or inflammation or from (2) general constitutional changes.

Local Trauma and Inflammation.—The unprotected portion of the bursa, situated under the deltoid muscle, is a weak point and is liable to direct trauma. Trauma may also be indirect and even obscure, and may include that due to overuse, sudden or unaccustomed use, sudden exertion in an attempt to keep from falling, pressure from an incorrectly applied bandage or fixation for relief of pain in the region of the shoulder after operations on the breast or the hand. Sudden motions may cause rupture of the muscle. Dislocations of the shoulder may also result in tearing of the tendinous attachments about the tuberosities. The bursa, being in intimate contact with these tendinous attachments, is always involved with marked disability.

General Constitutional Changes.—These include arthritis, advancing age and metabolic and nutritional disturbances. Bursitis associated with arthritis results from irritation by local arthritic osteophytes.

PATHOLOGIC PICTURE

The pathologic changes may be (1) bursal or (2) peribursal (musculotendinous).

Bursal Changes.—The bursa is a synovial sac subject to the same pathologic changes as is other serous tissue. Acute and chronic inflammation of the bursa results in thickening of the bursal walls, with formation of hypertrophic synovial villi, exudation of fluid and formation of adhesions.

Calcareous deposits¹⁰ when present in the bursa have ruptured into it from the underlying tendon in which they are formed. Such deposits do not originate in the bursa proper.

Peribursal Changes.—Lime Deposits: These deposits result from necrobiosis and calcification in the subjacent capsular and tendinous tissues and are demonstrable roentgenographically. As has been mentioned, there may be perforation of the deposits into the cavity of the bursa proper. In most cases, therefore, peribursal changes are found combined with changes in the bursa itself.

Painter¹¹ and Baer¹² explained the calcification as probably due to chronic inflammation in a tissue with little blood supply, undergoing necrosis with deposition of lime salts.

9. Footnote deleted.

10. Elmslie, R. C.: Calcareous Deposits in the Supraspinatus Tendon, *Brit. J. Surg.* **20**:190-196, 1932.

11. Painter, C. F.: Subdeltoid Bursitis, *Boston M. & S. J.* **136**:345-349, 1907.

12. Baer, W. S.: Operative Treatment of Subdeltoid Bursitis, *Bull. Johns Hopkins Hosp.* **18**:282-285, 1907.

Wright in 1908 reported a case (Codman's) of subdeltoid bursitis in which the condition was a slowly productive inflammatory process combined with degeneration and necrosis. He concluded that calcification in the supraspinatus tendon results from slight injury with an abortive attempt at repair in a tissue with little blood supply. These changes were again found by Wrede,¹³ who described necrobiotic changes in the tendon following rupture with calcification and formation of loose bodies.

Moschcowitz¹⁴ in 1915 reported his findings in 4 of Brickner's cases and concurred in the previous opinions held. The patients in these cases had been operated on for calcareous deposits in and around the subacromial bursa, associated with adhesive subacromial bursitis.

Lime deposits may be present in three forms: (1) as sandlike particles within the necrosed tissues, (2) as diffuse massive calcification of the necrosed tissue or (3) as isolated, discrete, sharply defined nodules embedded within the tendon or the granulation tissue. Calcification in some cases is on the surface of the tendon, in the form of a thick white gritty material associated with a minute tear of the tendon. On roentgen examination and at operation multiple deposits are found in the tendon at a distance from its insertion. The shadow in the roentgenogram may be formed by a deposit which is actually liquid. No connection has been found at any time between the calcification and the adjacent bone either on roentgen examination or at operation.

Tendon Rupture: Codman and Akerson¹⁵ in 1931 reported observations made at autopsy on 100 shoulder joints taken from 52 aged persons. This work was supplemented by the study of a second series of 100 shoulder joints in 1933. Rupture of the supraspinatus tendon was found in 39 per cent of these specimens. Normally the base of the bursa is as smooth, spherical and colorless as the cartilaginous surface of the head of the bone, but it has not the bluish luster of cartilage. Tears of the short rotators are visible after the roof of the bursa is incised. Rotation of the humerus brings various parts of the bursa into view. In the article by Codman and Akerson,¹⁵ Codman stated:

My own experience has led me to the conviction that rupture of the supraspinatus tendon is by far the most common cause of industrial shoulder disability and that complete rupture is a more painful, more serious, and more disabling lesion than fracture of the humerus or dislocation of the shoulder. It is the usual cause of traumatic subacromial (subdeltoid) bursitis.

13. Wrede, L.: Ueber Kalkablagerungen in der Umgebung des Schultergelenks: Ihre Beziehungen zur Periarthritis scapulo-humeralis, *Arch. f. klin. Chir.* 99:259-271, 1912.

14. Moschcowitz, E.: Histopathology of Calcification of the Spinatus Tendons as Associated with Subacromial Bursitis, *Am. J. M. Sc.* 150:115-126. 1915.

A. W. Meyer¹⁵ thoroughly investigated fraying of the long head of the biceps tendon and has published many articles explaining the changes in the tendons caused by attrition, with secondary changes resulting in calcification. He stated that excessive use of the shoulders by laboring men may by friction between the humerus and the acromion wear through the supraspinatus tendon and joint capsule and destroy the biceps tendon as it courses across the joint over the cartilaginous head of the bone.

ROENTGEN FINDINGS

Technic.—Positive roentgen findings have been reported by various authors, including Codman, Brickner,¹⁶ King and Holmes,¹⁷ Mumford and Martin¹⁸ and others. Roentgen examination should be made in all cases, whether the condition is of traumatic or spontaneous origin. Standard exposures of the shoulder are ample. The patient should be in the supine position, and the rays should be directed at the joint. Stereoscopic views, although not necessary in most cases, may be of value in showing whether or not a specific shadow is attached to the bone. It is imperative that roentgenograms be taken with the arm both in internal and in external rotation. The film taken with the arm in the position of external rotation is perhaps best made in the extreme of this motion with the arm abducted to an angle of 90 degrees and the hand lying at the head, palm up.

When motion at the shoulder is limited it may be impossible to obtain the optimum position for the taking of the roentgenograms. When one is searching for calcification care should be taken not to overexpose or overdevelop the films. The shadow, especially if it is small, may be obliterated on films that are too dark.

A comparative examination of the opposite (normal) shoulder must be made in all cases. Calcification has been found in the symptomless shoulder in cases in which none was present in the shoulder that was

15. Meyer, A. W.: Unrecognized Occupational Destruction of the Tendon of the Long Head of the Biceps Brachii, *Arch. Surg.* **2**:130 (Jan.) 1921; Spontaneous Dislocation and Destruction of the Tendon of the Long Head of the Biceps Brachii: Fifty-Nine Instances, *ibid.* **17**:493-506 (Sept.) 1928; Further Evidences of Attrition in Human Body, *Am. J. Anat.* **34**:241-267, 1924.

16. Brickner, W. M.: A Simple Easily Regulable Method of Applying Abduction in the Treatment of Shoulder Disability, *M. Rec.* **87**:15, 1915; Pain in the Arm: Subdeltoid (Subacromial) Bursitis; a Further Study of Its Clinical Types, Pathology, and Treatment, *J. A. M. A.* **69**:1237-1242 (Oct. 13) 1917.

17. King, J. M., Jr., and Holmes, G. W.: The Diagnosis and Treatment of Four Hundred and Fifty Painful Shoulders, *J. A. M. A.* **89**:1956-1960 (Dec. 3) 1927.

18. Mumford, E. B., and Martin, J. F.: Calcified Deposits in Subdeltoid Bursitis, *J. A. M. A.* **97**:690-694 (Sept. 5) 1931.

19. Footnote deleted.

the subject of the patient's complaints. The importance of such findings is obvious and is of great value in the proper interpretation of the problem.

In cases in which the deposit lies over the summit of the humerus it may be obscured by superimposition of the posterior portion of the acromion and the head of the humerus if films are taken by the routine method of directing the rays at right angles to the shoulder. The space



Fig. 1 (case 20, table 3).—*A*, roentgenogram taken preoperatively, showing calcification of the tendon and the bursa. *B*, roentgenogram taken postoperatively, showing the excellent results of the operative treatment.

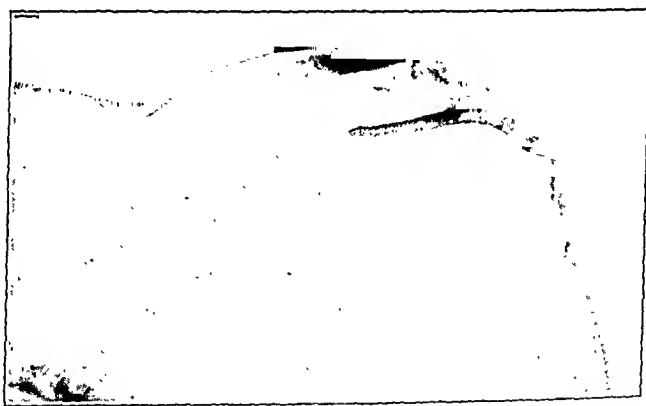


Fig. 2 (case 19, table 3).—Roentgenogram showing calcification of the tendon and of the floor of the bursa. Removal gave good results.

is best brought out in the film by directing the central ray caudalward and laterally by about 10 degrees in each direction. Increase of the angle caudally beyond 15 degrees may project the anterior lip of the acromion on the space in such a way as to simulate erroneously a large deposit. The usual location of the deposit is lower and ordinarily is not obscured by the acromion.

Roentgenographic Picture.—The presence of calcification (figs. 1 and 2) is evident on roentgen examinations. King and Holmes¹⁷ found

positive findings in 150 of 450 cases in which roentgen examination was done. Mumford and Martin¹⁸ found deposits in 14 of 16 cases.

When studying the roentgenograms in a case of subacromial bursitis one should keep the following facts in mind:

1. Roentgen evidence of pathologic change is not present in all cases. Whereas films showing definite evidence of pathologic change are of significance in establishing the diagnosis, normal roentgenograms are of no aid in differentiating or eliminating the disease, and one must rely for correct diagnosis entirely on the history, physical findings and progress of the lesion.

2. Changes in the soft tissues are due to areas of calcification in the tendinous tissue underlying the bursa. The visible shadow in the roentgenogram is adjacent to the greater tuberosity of the humerus and may vary in size from a pinpoint shadow to a large shadow 1 inch



Fig. 3 (case 3, table 3).—Roentgenogram showing an avulsion fracture of the greater tuberosity. The results of treatment were good. A trichina cyst of the supraspinatus tendon was found at operation.

(2.5 cm.) or more in diameter. The shadow may represent a single large deposit or a collection of many small deposits in the area.

3. Chip fractures of the tuberosities (fig. 3) lying in the soft tissues adjacent to the humerus are differentiated by the denser shadow which they cast on the films and by their sharpness of outline. A defect in the humerus at the site of the fracture may be discernible in some cases. In cases of fracture of long standing the differentiation may be more difficult, as the shadow may be rounded and have a hazy appearance; but it may then be easier to recognize the site of fracture in the humerus, as there may be some rarefaction to accentuate the defect.

4. The anterior lip of the acromion may be superimposed on the clear space usually appearing between the acromion and the humerus. The fact that the clavicle will be seen to articulate with the shadow will serve to differentiate it from a large deposit and to identify it as the acromion.

5. Atrophy of the proximal end of the shaft, with subchondral cysts, may be found in association with both arthritis and bursitis and may also be caused from disuse. The differentiation cannot be made entirely on the basis of the roentgen findings. Evidence of arthritis in other joints may aid in the differentiation. The presence of bony exostoses (fig. 4), either arthritic or developmental, is important. These may be responsible for concomitant bursitis. Their surgical removal may result in sensational disappearance of symptoms and return of function.

6. Other pathologic conditions, such as metastases from malignant lesions, primary malignant lesions of the bone, infection of the bone and localized areas of rarefaction, such as may be associated with leukemia and Hodgkin's disease, may be demonstrable roentgenographically. The possibility of such lesions must always be watched for and their presence recognized.



Fig. 4 (case 21, table 3).—Roentgenogram taken after an operation, showing removal of an exostosis of the tuberosity. The results of the operation were good.

7. Diagnostic errors arising from failure to make exposures with the arm in both external and internal rotation are inexcusable in examination of the shoulder, not only for bursitis but for any lesion that may be suspected. Such exposures give views of the humerus in the anterior-posterior and lateral positions.

8. Calcification without symptoms is occasionally found and, as has been commented on, may indicate a previous injury. Comparative studies of the normal shoulder are therefore necessary for proper interpretation. Carnett²⁰ reported deposits in as many as 25 per cent of symptomless shoulders. He concluded that this probably indicates an

20. (a) Carnett, J. B.: So-Called Calcifying Subacromial Bursitis, *Radiology* 17:505-513, 1931. (b) Carnett, J. B., and Case, E. A.: A Clinical and Pathological Discussion of So-Called Subacromial Bursitis, *S. Clin. North America* 9:1107-1126, 1929.

earlier bilateral lesion. Deposits may appear later in the painful shoulder, as the early complaints may be entirely due to inflammation and the examination may have been made before the deposits were laid down.

9. Free bodies in the joint, of synovial or bony origin, may be confusing. These may be attached to the synovia and thus may not show change of position in successive roentgenograms. The position of the bodies and failure of the condition to respond to physical therapy should aid in the roentgenographic differentiation.

SYMPTOMS

The symptoms of subacromial bursitis vary greatly and are modified by the cause and the complexity of the pathologic changes. A classification of the different types of this condition can be accepted only if the symptoms are correlated with the pathologic process involved. Various classifications are made by different authors on the basis of roentgen and clinical findings, but all these fall into the various pathologic groups.

From his observation of cases of subacromial bursitis Codman has classified the condition into the following clinical types: (*a*) acute spasmodic bursitis, (*b*) subacute adhesive bursitis, (*c*) chronic nonadhesive bursitis, and (*d*) bursitis due to complete tendon rupture. Bursitis due to partial tendon rupture may come under any one of the first three forms, depending on the extent to which the bursa is involved. This classification is based on the physical findings which, in turn, are determined by the underlying pathologic process.

Acute Spasmodic Bursitis.—Patients with this type of bursitis present themselves with local evidence of inflammation, pain, tenderness and secondary muscular spasm. Serous tension and calcium deposits may or may not be present as a result of the acute inflammation of the bursa. Bursitis due to acute partial tears of the tendons may be of this type. The shoulders in such cases are locked by reflex spasm (scapulohumeral spasm), and free motion is limited to an arc of about 10 degrees. Acute partial tears of the supraspinatus tendon give rise to the same symptoms. Patients with this type of bursitis maintain the shoulder in a sling, and the condition therefore tends to become subacute or chronic.

The tenderness found is usually below the acromion to the outer side of the bicipital groove. It may be localized over one point or may be diffuse over the entire bursa, its location depending on the nature of the injury. When the condition is associated with a tear in the supra-

spinatus tendon, tenderness is on the greater tuberosity, which is the point most prominent and also most vulnerable, as it is poorly covered by muscle.

In the absence of adhesions the tenderness will disappear under the acromion when the arm is abducted beyond 90 degrees. This is called Dawbarn's sign.

Pain may extend down the outer side of the arm into the hand and fingers or to the cervical region, or it may be confined to the region of insertion of the deltoid muscle. It may be constant, may become worse at night and may make it impossible for the patient to sleep on the affected side. Exacerbation of the pain during inclement weather is not uncommon.

Effusion into the bursa, when it occurs, is difficult to palpate, as it is covered by muscle. It may, however, sometimes be demonstrable by puffiness over the bursa.

Motion of the arm may be limited because of the associated pain as well as by actual spasm or adhesions.

Codman in 1912 offered the following clinical test to aid in differentiating muscular spasm from true adhesions. The patient with acute spasmodic bursitis cannot abduct the arm because of the protective muscular spasm which wards off the associated pain. However, he can bend forward with the knees straight and with the finger tips to the floor. In this position the humerus is abducted on the scapula by gravity alone, without any muscular effort. Therefore, in such cases the arm can be raised over the head as the patient rises, although such motion was considered impossible of execution.

CASE 1.—C. W., a man aged 57, came to the clinic complaining of pain in the right shoulder and limitation of motion of eight months' duration. The onset was gradual and was not associated with any trauma. The pain radiated down the arm to the wrist and was worse when the weather was inclement. Physical examination showed some limitation of all motions about the shoulder, due to reflex spasm from pain. Abduction and external rotation were especially restricted. A point of tenderness was present over the greater tuberosity in the region of insertion of the supraspinatus tendon. Roentgenograms showed atrophy of the proximal end of the humerus. A diagnosis of subacromial bursitis was made. Treatment consisted of physical therapy. Complete relief of symptoms was obtained in two weeks.

CASE 2.—E. A., a girl aged 17, entered the clinic with a history of direct trauma to the shoulder three and one-half months prior to entry, resulting in a sternoclavicular dislocation which had been treated by immobilization in adduction for three weeks. The complaints were pain in the shoulder and limitation of motion, especially abduction and external rotation. A tender spot was present over the greater tuberosity. Treatment consisted of the injection of 5 cc. of a 2 per cent solution of procaine hydrochloride into the bursa. After this treatment a more complete range of motion was possible. The injection was repeated within a

week. The arm was kept in an abduction splint and was treated with physical therapy. Full range of motion and complete relief from pain followed in three and one-half months.

Subacute Adhesive Bursitis.—This type of bursitis in which actual adhesions are present between the roof and the floor of the bursa is a result of progression of acute spastic bursitis. There is an actual mechanical limitation of motion, especially of abduction and external rotation. The limited motion greatly diminishes the amount of pain. Atrophy of the muscles about the shoulder joint and possibly of the entire arm may be present. As has been mentioned previously, the Dawbarn sign is usually absent, as motion is too limited to allow the tuberosity of the humerus to pass under the acromion. Approximately 10 degrees of free motion in the joint is also present in such cases, with additional motion resulting from movement of the scapula.

CASE 3.—R. K., a woman aged 42, entered the clinic with pain in the left shoulder and limitation of motion. She had landed on her arm in an attempt to guard herself in a fall five months previously. No treatment was given for three months; then the arm was treated by rest in a sling for six weeks. When the patient was admitted to the clinic a slight degree of motion of the shoulder was present in all directions except that of outward rotation. Abduction was limited to 60 degrees. A tender spot was present over the subacromial bursa. Roentgenograms showed no pathologic process. A diagnosis of adhesive bursitis was made. The shoulder was manipulated (with the patient under a general anesthetic) into abduction and outward rotation and was then placed in a platform splint. Physical therapy was given. Six weeks after the manipulation the condition of the patient was definitely improved.

Chronic Nonadhesive Bursitis.—This type of bursitis follows absorption of some of the adhesions of the subacute lesions in the process of healing. The previous acute inflammation of the bursa leaves the walls roughened and thickened. In such cases the symptoms are prolonged and have exacerbations over a period of years. Motion is good, but pain results when a full arc of movement is attempted. The variability of the points at which intermittent pain occurs is due to irregularities and roughened areas of the bursa passing under the acromion. This pain may radiate to the cervical region or to the point of insertion of the deltoid muscle. As a result motion of the shoulder is uneven and jerky but is free of scapular movement.

Tenderness may or may not be present. However, if it is present the Dawbarn sign is also present. Abduction and external rotation are only slightly limited, but at some point in abduction painful locking occurs; it will disappear on further abduction. This pain is referred to as Codman's sign.

CASE 4.—H. B., a man aged 56, entered the clinic complaining of pain and limitation of motion since straining the arm four weeks previously. A similar

incident had also occurred two years earlier, but the condition subsequently cleared. Some tenderness was present over the great tuberosity. Slight atrophy of the supraspinatus muscle was also present. Abduction was free to 90 degrees, at which point an impediment and jar resulted in pain, after which abduction could be continued (Codman's sign). Treatment with an abduction splint and physical therapy gave some improvement in two months.

Bursitis Due to Partial Tears of the Supraspinatus Tendon.—This injury may give rise to bursitis of the first three types as follows: If the tendon is barely nicked and only a few tendon fibers are involved, acute spastic bursitis results; this may develop into subacute adherent bursitis. With healing, simply a little residual notch in the bursa may be left; the original symptoms may subside, and chronic nonadherent bursitis may result.

Bursitis Due to Complete Tendon Rupture.—It is of prime importance to recognize complete tendon tear. It usually occurs in laborers over the age of 40, who have no complaints before the accident and in whom an adequate injury is followed by immediate sharp pain with loss of power to induce abduction. With complete laceration of the supraspinatus tendon, abduction cannot be completely maintained even against feeble downward pressure on the arm. The deltoid muscle cannot initiate or maintain abduction unless the supraspinatus muscle holds the head of the humerus firmly in the glenoid fossa.

A local tender spot is present at the tip and lateral aspect of the acromion. Palpation of a sulcus may be possible at the point of rupture, as the tendon is retracted. This may also indicate the presence of a deposit. A sharp pain is elicited as the defect in the tendon passes under the acromion during abduction of the arm (at about 30 to 50 degrees).

CASE 5.—H. B., a man aged 61, entered the clinic four weeks after a sudden jerk of the arm was followed by sudden, sharp pain in the shoulder and by restriction of abduction to 15 degrees. A tender spot was present at the insertion of the supraspinatus tendon. Treatment for three weeks after admission, with physical therapy and an abduction splint, resulted in no improvement. Operation showed rupture of the supraspinatus tendon, which was found curled up under the acromion. Repair was followed by loss of pain and complete return of function in three months. This patient has now been observed for four years and ten months. He states that he believes the shoulder which was operated on to be stronger and better than the opposite shoulder.

CLINICAL ANALYSIS OF A SERIES OF TWO HUNDRED AND EIGHTY-EIGHT CASES

In analyzing the series of 288 cases from the orthopedic department of the State University of Iowa, I have not divided them into groups except as to type of onset, because the various types of subacromial bursitis blend into each other, as indicated in the preceding section on symptoms.

Age Incidence and Onset.—The age incidence and the relation of age to onset are shown in table 1. The greatest incidence is between the ages of 40 and 70. Of the patients with traumatic bursitis only 3 were under 20. The youngest of these was 16. Of the patients with non-traumatic bursitis 5 were under 20. The youngest of these was 17. Constitutional changes as well as trauma may take their toll early in life. Trauma is seen to play an important role as the cause of the pathologic changes which in cases of nontraumatic bursitis must result from constitutional deficiencies, age and nutritional disturbances.

Sex.—Sex does not play an important role. Of 285 patients, 149 were male and 136 were female. This indicates an essentially equal incidence.

Extremity Involved.—In a total of 280 cases the right shoulder was involved in 165, the left in 102 and both shoulders in 13. The greater

TABLE 1.—*Relation of Onset to Age Incidence*

Age Groups, Years	Onset			Totals for Each Age Group
	Traumatic: Direct and Indirect	Non-traumatic	Not Noted	
10-20.....	3	5	1	9
20-30.....	17	23	0	40
30-40.....	10	6	1	17
40-50.....	23	27	0	50
50-60.....	45	37	1	83
60-70.....	29	27	0	56
70-80.....	6	4	0	10
Over 80.....	0	0	1	1
Not noted.....	4	17	1	22
Totals.....	137	146	5	288

incidence for the right arm is probably due to the fact that this limb is generally subject to more exposure and use both in industry and in sport.

Arthritic Changes.—Of 288 patients, 47, or 16 per cent, had evidence of arthritis either in the shoulder or in other parts. Of the total number of patients, 15, or 5 per cent, showed localized evidence of arthritis in the shoulder. The incidence of arthritis is important as a complication of bursitis and is a factor in prognosis.

General Symptoms and Findings.—Table 2 shows the incidence of general symptoms and findings.

(a) Pain varied in severity but was present in all cases.

(b) Radiation of the pain was to the insertion of the deltoid muscle, the neck and down the arm to the wrist and hand.

(c) Atrophy may involve the supraspinatus, the infraspinatus and the deltoid muscle. It varies with the duration of the disability and with the degree of fixation of the shoulder.

(d) The pressure point over the greater tuberosity may be small or may be diffuse over the entire bursa. Its extent is indicative of the amount of inflammation and the resultant disability.

(e) Restriction of motion was present in 95 per cent of cases. Abduction and external rotation are the motions most commonly affected. Some motion persists in all such cases; this differentiates the condition from the "frozen shoulders" associated with arthritis.

(f) Roentgen findings are an important aid in diagnosis. Repeated examinations and comparative studies of both shoulders are desirable in all cases.

TABLE 2.—Incidence of General Symptoms

	Incidence		Total Number
	Number of Cases	Percentage	
Cases studied.....	258
Pain.....	238	100	
Radiation of pain.....	43	15	
Muscular atrophy.....	58	20	
Pressure point over greater tuberosity.....	169	58	
Cases studied for limitation of motion.....	264
Limitation of motion.....	251	95	
Abduction alone.....	88	35	
External rotation alone.....	11	4	
Internal rotation alone.....	1	1—	
Abduction and external rotation.....	71	28	
Abduction and internal rotation.....	12	4	
External and internal rotation.....	3	1	
All motions restricted.....	65	26	
Roentgen examinations.....	154
Positive findings.....	77	50	
Osteification.....	23	15	
Atrophy.....	34	22	
Local arthritis.....	15	10	

DIFFERENTIAL DIAGNOSIS

Although subacromial bursitis may coexist with many other lesions, it must be differentiated from certain conditions as follows:

Fractures.—Immediately after trauma the presence of fractures of the tuberosities, fractures of the surgical and anatomic neck of the humerus and fractures of the clavicle can be easily discovered by the characteristic roentgen findings of these conditions and by the presence of ecchymosis and swelling on the inner side of the arm. With adequate roentgenograms, fractures should never be overlooked.

Dislocation.—Dislocation of the head of the humerus, as well as acromioclavicular separation, are easily differentiated from subacromial bursitis by the roentgen and physical findings characteristic of these lesions. Inflammation and involvement of the bursa may be present immediately after the injury, or it may not appear until after prolonged immobilization of the shoulder or until mobilization is resumed. Bur-

sitis becomes manifest by the continued presence of disability and by physical findings which are characteristic of it but cannot be explained by the original lesion.

Tumors About the Shoulder.—Malignant tumor, giant cell tumor and cystic disease of the bone may be present in the upper end of the humerus and may cause secondary involvement of the bursa. Such lesions are of uncommon occurrence in the clavicle and scapula. Pain and limitation of motion may be the only early symptoms and may thus simulate the early stages of bursitis. Such symptoms in a patient under the age of 20 should be watched carefully for possible giant cell tumor. A persistent, growing tumor mass is characteristic. The characteristic roentgen findings will aid in identifying such lesions.

Tuberculosis.—The differential diagnosis of tuberculosis may be difficult. Tuberculous invasion takes place about the intertubercular notch and therefore involves the short rotators and the bursa so that fixation of the shoulder results. However, the roentgen picture is characteristic. The atrophy of the muscles about the shoulder is more generalized and more marked than in cases of bursitis, and there may be no motion whatever about the shoulder. The slight degree of motion always present with bursitis proper is absent with tuberculosis.

Syphilis.—Although such a condition is rare, syphilitic involvement of the shoulder may be present. Differentiation depends on the history, the Wassermann reaction, the roentgen findings and the presence or absence of signs of syphilis elsewhere.

Arthritis.—The bursa may be involved in cases of chronic arthritis either of the atrophic or of the hypertrophic variety. Atrophic arthritis gives rise to symptoms of true inflammation, local tenderness, complete loss of motion, a more obtuse angle between the scapula and the shaft and frequent involvement of other joints. Hypertrophic arthritis produces bursitis because of irritation of the bursa caused by the existing exostosis. In cases of arthritis the capsule is found to be tender in the axilla.

The frozen shoulder caused by spasm or adhesions must be differentiated from the frozen shoulder caused by arthritis. The midposition of arrest of the shoulder due to arthritis is in 25 degrees flexion and forward motion, so that when the arm is at the side the vertebral border of the scapula is no longer straight down but points medially in midline. This finding is never present in the frozen shoulder associated with bursitis. This position is described by Lange.

Acromioclavicular arthritis is characterized by local tenderness at the joint with a possible luxation and thickening; these symptoms are helpful in differentiation of the lesion from bursitis.

Sprain of Adductor Insertions.—In cases of trauma involving the region of insertion of the pectoralis major and latissimus dorsi muscles, pain on external rotation is entirely limited to the inner side close to the axillary fold and can be elicited by palpation. In cases of trauma to the subscapularis tendon, the tenderness is located over the lesser tuberosity.

Brachial Neuritis.—Codman stated that there is no such thing as brachial neuritis and that the pain in the arm is due to traumatic or inflammatory changes in the subacromial bursa or in the surrounding musculotendinous tissue. He concluded that herpes zoster may be the manifestation of true neuritis.

Injuries of the Biceps Tendon.—The biceps tendon is well protected beneath the bursa and the tendinous expansion of the supraspinatus muscle. According to Codman, severe direct trauma to the capsule, including its rupture, is necessary to injure or displace the biceps tendon. Yet Meyer²⁵ has repeatedly reported evidence of attrition of this tendon. Rupture does occur, and it may take place at the tendinous insertion, at the site of union of the muscle and the tendon or in the intertubercular sulcus (the most frequent site), with resultant degenerative changes in the tendinous tissue as a complement of arthritis. Inflammation of the sheath of the biceps tendon may simulate subdeltoid bursitis. All motions of the humerus involve motion of the tendon in its sheath. Lesions of the sheath may occur, and when they are present the tendon does not move within the sheath. Inflammation of the sheath results in symptoms of bursitis. The local tenderness in such cases is in the bicipital groove. Whereas forward and backward motion may be free in cases of bursitis, the bicipital tendon is called into vigorous play in these motions, and the presence of even 10 degrees of painless motion in these directions indicates absence of inflammation of the sheath of the biceps tendon.

TREATMENT

Conservative Treatment.—The patient with acute bursitis without deposit of calcium is treated conservatively by means of opiates and sedatives, rest, abduction, heat and diathermy and also with passive motion within the range of comfort. Steindler²³ concluded that foci of infection play a contributing role in the production of all such lesions and should by all means be checked and removed when present. It is not the purpose of this paper to discuss the general importance of such

23. Steindler, A.: *Reconstructive Surgery of the Upper Extremity*, New York, D. Appleton and Company, 1923; *Subacromial Bursitis*, read before the American Academy of Orthopedic Surgeons, Jan. 14, 1936; personal communications to the author.

foci, but for lesions so closely associated with arthritis the removal of infective foci seems logical and rational.

Opiates and sedatives for the relief of the actual pain will relieve the anxiety of the patient and of the family and will make for better cooperation between the patient and the physician. It will also make it much easier to proceed with conservative measures and to give them an adequate trial.

As with acute inflammation elsewhere in the body, rest is of prime importance. For the patient with mild bursitis, rest of the shoulder in a sling is sufficient. For one with more severe bursitis, immobilization of the shoulder in an abduction splint with the arm in abduction and outward rotation is more desirable and should be employed in spite of the inconvenience that attends keeping the arm in this position. The abduction splint permits relaxation of the rotators and allows the tender point on the base of the bursa to avoid making contact at the acromion. The use of the abduction splint was described by Monks as early as 1890.

The recumbent abduction position of Brickner is admirably suited for the patient with spasticity of the muscles and for one who is bed-ridden or who prefers being in bed to walking around with an abduction splint. The patient remains in bed with the arm abducted as much as is comfortably possible. The arm is supported by a pillow; a muslin loop is attached from the wrist to the head of the bed, and the upper end of the bed is elevated. The body will gradually slide to the foot of the bed and the arm will travel relatively farther and farther up. Thus a shoulder resistant to forcible abduction will yield to gradual countertraction without pain to the patient. It may take a week or more in some cases but, according to Brickner, the spasm may sometimes be overcome in as short a time as twenty-four hours. This treatment may also be reserved for use only at night and may be alternated with the use of the abduction splint. Brickner did not recommend this gradual traction in cases in which it proves to be painful or fails to give prompt increase in the range of motion.

Heat, mild massage and passive motion, especially with the patient in the stooping position, are beneficial and should be administered. The extent of passive motion should always be limited so as not to produce any pain. Injection of procaine hydrochloride may be used to relieve pain and spasm, to help in the differentiation of the condition from true adhesive bursitis and to help in overcoming spasticity before the arm is placed in abduction.

For acute bursitis presenting localized symptoms, irrigation of the bursa with saline solution has completely relieved the symptoms. Using

the technic of Smith-Petersen, Patterson and Darrach²⁴ insert two needles into the bursa, after anesthetizing the skin with procaine hydrochloride, and lavage the bursa with about 2 ounces (60 cc.) of saline solution. The bursa may be approached through the anterior and also through the anterolateral portion of the deltoid muscle, as is also described by Steindler. Patterson and Darrach obtained calcium salts in the lavage even in cases in which the roentgen findings were negative. From anatomic studies it might appear almost impossible to enter the bursa in this manner; but in the presence of pathologic changes the walls of the bursa are thickened and the sac is widened from the tension. This makes entry easier than might be anticipated.

Injection of sclerosing and antiseptic solutions into the bursa has also been attempted, as was reported by Fields,²⁵ who injected a 5 per cent solution of iodoform into the bursal sac. This treatment has not been accepted.

Diathermy has given excellent results in the hands of many and is perhaps the most efficacious of the physical means of treatment. Deering²⁶ claimed priority in 1916 for the first recorded attempt to treat the lesion "by means other than drugs, surgery, or orthopedic measures." Mumford and Martin reported good results in 16 cases. Coopermann, Resnik,²⁷ Harris and Titus,²⁸ among others, have reported excellent results following diathermy treatment of the calcifications, with absorption after the treatment.

Roentgen treatment too has been used with good results and deserves consideration. I have had no personal experience with this form of treatment. The amount of exposure given is not a barrier to subsequent surgical treatment and may be considered before surgical intervention is tried although perhaps not until all other conservative measures have failed to give relief. Lattman²⁹ in a recent report described the following routine technic which has given good results in his hands: 350 roentgens at 200 peak kilovolts, filtered with 0.25 mm. of copper, was given through a port 15 cm. square at a distance of 50 cm. This dose was applied to both the anterior and the posterior

24. Patterson, R. L., and Darrach, W.: Treatment of Acute Bursitis by Needle Irrigation, *J. Bone & Joint Surg.* **19**:993-1002, 1937.

25. Fields, S. O.: Subacromial Bursitis, *New York M. J.* **101**:163, 1915.

26. Deering, G. E.: Physical Treatment of Subacromial Bursitis, *Phys. Therap.* **48**:362-366, 1930.

27. Resnik, J.: Physiotherapy in Subdeltoid Bursitis, *Phys. Therap.* **47**:322-329, 1929.

28. Titus, N. E.: Electrical Treatment of Subdeltoid Bursitis, *Am. J. Surg.* **6**:318-334, 1929.

29. Lattman, I.: Treatment of Subacromial Bursitis by Roentgen Irradiation, *Am. J. Roentgenol.* **36**:55-60, 1937.

aspect of the shoulder. The symptoms may be aggravated during the first twenty-four hours after such treatment, but a definite decrease of pain and increase of mobility appear in the second twenty-four hours. One such exposure usually suffices, but a second treatment may be necessary for complete relief. Lattman gave this treatment in 20 cases in which the patients have been followed from one to five years.

Acute bursitis judiciously treated, with early movement and no prolonged fixation, may be cured within a few weeks.

Manipulative Treatment.—If after two or three months of conservative treatment there is no improvement, it is usually because there are adhesions either without much fixation or with a frozen shoulder. Careful manipulation of the shoulder, that is, stretching without use of force, is beneficial. Attempts to force the adhesions do not give good results and may even result in a tear of the subscapularis tendon. After such manipulation the arm should be maintained in abduction and outward rotation in order to keep the adherent surface apart and opposite healthy tissues. It is preferable to incise down on and cut the adhesions rather than to use force to free them.

For adhesions that are still plastic, the spasm from pain being the main cause of the limitation of motion, treatment should follow the lines of that for acute bursitis with spasm. Adhesive bursitis associated with tendinitis is usually cured in from six to twelve months of conservative treatment, although it may persist for two years if there are secondary contractures.

Operative Treatment.—Bursa: Immediate incision and relief of tension or removal of the deposit has been recommended by Codman, Brickner, Carnett, Ferguson,³⁰ and Haggart and Allen.³¹ Steindler and Campbell, among others, concluded that conservative measures should be used and that indications for more radical treatment should be made only on specific findings or on failure of conservative measures to give adequate improvement.

The operation for exploration or drainage of the calcification necessitates only a small incision over the tuberosity. The deltoid fibers are separated, and the bursa is notched. The niche may be enlarged for exploration of the floor of the bursa, and as the arm is rotated the short rotators can be seen at the head. The calcified material appears as a deep red, circular zone on the base of the bursa, with a whitish mound in the center. When this is opened, the calcified material will exude

30. Ferguson, L. K.: Painful Shoulder Arising from Lesions of the Sub-acromial Bursa and Supraspinatus Tendon, *Ann. Surg.* **105**:243-256, 1937.

31. Haggart, G. E., and Allen, H. A.; Painful Shoulder: Diagnosis and Treatment with Particular Reference to Subacromial Bursitis, *S. Clin. North America* **15**:1537-1560, 1935.

as though under pressure. All available material should be curetted out, and all adhesions within the bursa should be cut or broken. Part of the roof may be excised and the wound closed. Haggart and Allen³¹ give active exercises within forty-eight hours, with the application of heat and hot fomentations. They allow their patients to be up on the third day and have had no recurrences in 25 cases in which operation was performed.

Both calcified deposits and osseous overgrowths may cause irritation and may give mechanical difficulties as impediment to motion. In such cases operative removal is indicated and is necessary before any relief can be expected.

Tendon Repair: Complete rupture of a tendon necessitates operative repair unless operation is contraindicated by the general condition of the patient. The technic developed by Codman and by Wilson³² gives good results. General anesthesia is best employed with the patient lying on his back; a sandbag is placed under the scapula to make the greater tuberosity as prominent as possible. It is desirable to explore the bursa and to determine the extent of the lesion before proceeding with a wider exposure of the tendon. For this purpose a small incision is made, about 2 inches (5 cm.) in length, extending downward from the acromioclavicular joint and splitting the fibers of the deltoid muscle. It should not be extended farther, as there is danger of severing the anterior portion of the axillary nerve and causing paralysis of the anterior fibers of the deltoid muscle. The bursa is entered, and with rotation and traction on the arm the greater and lesser tuberosities and the tendinous attachments can be visualized. A rupture appears as a gap in the capsule, through which the articular cartilage of the head is visible. When the rent is small the tendon can be pulled from under the acromion with a forceps and sutured to the tuberosity. With a larger gap a wide exposure of the tendon is necessary. For this, Codman's saber-cut incision is used. This incision passes posteriorly over the top of the shoulder from the acromioclavicular joint. Wilson divides the articulation and cuts through the acromion with a saw to give a wide exposure. A channel is made in the anatomic neck of the humerus and the inner face of the greater tuberosity, and several drill holes are made through the greater tuberosity into the channel. The fibrous edge of the tendon is excised, and with the arm in abduction the tendon is approximated to the channel and sutured in place through the drill holes with sutures of silk or of fascia lata. The acromion is sutured to the clavicle with catgut. It is not necessary to suture the divided fragments of the acromion.

32. Wilson, P. D.: Complete Rupture of the Supraspinatus Tendon, *J. A. M. A.* 96:433-439 (Feb. 7) 1931.

Postoperative fixation in a platform splint should be maintained for three weeks; this should be followed by daily removal of the splint and by discontinuance of its use by the end of four weeks. There is usually a complete return of function in from three to four months after adequate massage and physical therapy have been given.

Operation was performed in 21 of the present series of cases. A summary of the data is given in table 3. The patient in case 1 showed rupture of the tendon of the supraspinatus muscle and rupture of the long head of the biceps tendon. The former was repaired, but the ends of the biceps tendon could not be located. The result of the operation was good; there was complete return of function.

TABLE 3.—*Summary of Cases in which Operation Was Performed*

Case No.	Patient	Pathologic Condition	Period of Observation	Result
1	H. B.	Rupture of the supraspinatus tendon.....	4 yr. 10 mo.	Good
2	J. B.	Rupture of the supraspinatus tendon.....	2 yr.	Good
3	J. M.	Trichinosis affecting the supraspinatus muscle		
		avulsion fracture of the greater tuberosity....	4 yr. 5 mo.	Good
4	W. S.	Contractures of the latissimus dorsi and pectoralis major muscles.....	5 yr.	Good
5	T. K.	Rupture of the subscapularis tendon.....	10 mo.	Improvement
6	M. F.	Rupture of the long head of biceps tendon.....	3 yr. 7 mo.	Improvement
7	W. S.	Rupture of the long head of the biceps tendon (repaired May 1937)		Poor
8	C. C.	Adhesive bursitis.....	8 mo.	Good
9	H. L.	Adhesive bursitis.....	7 mo.	Good
10	J. M.	Adhesive bursitis.....	2 mo.	Improvement
11	H. M.	Adhesive bursitis.....	11 mo.	Poor
12	J. S.	Adhesive bursitis.....	8 mo.	Poor
13	A. S.	Adhesive bursitis.....	14 mo.	Good
14	H. C.	Adhesive bursitis.....	17 mo.	Poor
15	A. A.	Adhesive bursitis.....	2 yr. 4 mo.	Poor
16	R. G.	Adhesive bursitis.....	2 mo.	Improvement
17	W. H.	Adhesive bursitis.....	2 mo.	Poor
18	D. H.	Adhesive bursitis.....	2 mo.	Improvement
19	C. H.	Calcifications.....	1 yr. 7 mo.	Good
20	J. H.	Calcifications.....	3 mo.	Good
21	F. J.	Exostosis of the humerus.....	1 yr. 5 mo.	Good

Examination of a specimen from the supraspinatus muscle in case 3 showed typical *Trichina spiralis*. The muscle appeared intact on gross examination at operation.

Repair of the biceps tendon in case 6 was successful. However, at the time of writing there is still restriction of motion of the shoulder. The patient in case 7 underwent the third operation at the time this paper was written. Fascial reinforcement was employed in the last operation in an attempt to make the repair hold.

The poor results in cases 12, 15 and 17 were due to osseous changes found on operation and in subsequent follow-up roentgenograms.

A second operation for reefing of the joint capsule was necessary in cases 10, 19 and 20.

Tenotomy of the latissimus dorsi and pectoralis major muscles was performed for relief of contractures in case 4. The operation was followed by complete return of the function of the shoulder.

The patient in case 21 (fig. 4) was operated on for a possible tear of the supraspinatus tendon. An exostosis of the tuberosity was found which impinged against the acromion in abduction. Its removal was followed by complete return of function and disappearance of symptoms. Preoperative roentgenograms had failed to show the exostosis.

END RESULTS

The incidence of results in all the cases in which treatment was given (168) is shown in table 4. The cases in which operation was performed include those in which the condition had failed to respond to conservative measures.

CONCLUSIONS

1. Subacromial bursitis may be due to a primary pathologic process in the bursa proper, or it may be secondary to a pathologic process in

TABLE 4.—*Treatment and Results in One Hundred and Sixty-Eight Cases*

	Number of Cases	Percentage
Nonoperative treatment.....	147	87
Operative treatment.....	21	13
Results with nonoperative treatment		
Cured.....	102	69
Improvement.....	28	19
No improvement.....	17	12
Results with operative treatment		
Cured.....	10	48
Improvement.....	5	24
No improvement.....	6	28

the musculotendinous cuff or in the bones of the shoulder joint. The changes may be of (1) traumatic, (2) arthritic or (3) infectious origin. Thus direct blows, overuse, strains, disuse, constitutional changes or irritation from arthritic bony overgrowths may be the causative factor. Arthritis was present in 16 per cent of the present series of 288 cases. As a rule patients with bursitis are past the age of 40. However, the condition may appear much earlier. In this series the youngest patient with bursitis due to trauma was 16, and the youngest patient with nontraumatic bursitis was 17.

2. The most common clinical findings in the 288 cases were: (1) pain in all, (2) restriction of motion in 95 per cent, (3) a pressure point over the greater tuberosity in 58 per cent and (4) muscular atrophy in 20 per cent. Roentgen examination in 154 cases showed atrophy of the proximal end of the humerus in 22 per cent, calcification in the region of the bursa in 18 per cent and local arthritic changes in 10 per cent.

Radiation of the pain to the insertion of the deltoid muscle, to the cervical region, and down the arm to the wrist and hand was present

in 15 per cent of cases. Of the 95 per cent of patients with restriction of motion, 35 per cent had restriction of abduction alone, 28 per cent had restriction of abduction plus restriction of external rotation, and 26 per cent had restriction of all motion. Restriction of the other motions accounted for the remaining 10 per cent.

3. Conservative measures, including physical therapy, the use of an abduction splint and manipulation, gave good results in 69 per cent of 168 cases, improvement in 19 per cent and poor results in 12 per cent. Operation in 21 cases resulted in cure in 10, or 48 per cent; improvement in 5, or 24 per cent, and no improvement in 6, or 28 per cent.

4. Operative intervention should be reserved for cases of bursitis due to complete tendon rupture and for cases in which the condition does not respond to conservative measures.

Complete tendon rupture can be recognized by its onset with sudden sharp pain, loss of power to induce abduction and the presence of a tender spot at the tip and lateral aspect of the acromion.

metriosis. Strongin stated that these tissues begin to function when stimulated by hormonal activity (probably gonadotropic) caused by the removal of some inactivating factor. In my case and similar cases the removal of the endometrium, incident to hysterectomy, might conceivably be the initiator of such an imbalance.

REPORT OF A CASE

A Swedish woman aged 49, unmarried, was admitted to the New York Hospital April 15, 1935. In 1933 a hysterectomy had been performed at the Woman's Hospital of New York City, for myomas of the uterus. Amenorrhea had been present until eighteen months previous to the current admission. At that time she began to have periodic bleeding from the umbilicus, associated with numbness about this area. The attacks were introduced by prodromes similar to those which had preceded the previous menstrual periods, namely, slight cramplike abdominal pain, languor and mild headache. The attacks occurred roughly every twenty-eight days and lasted from three to four days. The quantity of discharge was always small. At no time was there bleeding per vaginam. She suffered from mild hypertension and had had the right eye enucleated some years previously, because of chronic inflammation.

On examination the umbilicus was seen to be moderately enlarged and deepened. The surrounding tissues were pigmented dark brown for a distance of 3 cm. The base of the umbilicus was formed by a firm, warty mass which showed no tenderness to palpation. The old scar from hysterectomy was well healed and did not extend to the umbilicus.

On April 16 the umbilicus was excised, with an elliptic section of the surrounding tissues, down to and through the peritoneum. The postoperative course was uneventful.

Pathologic Observations.—The specimen measured 14 by 22 cm. and contained the umbilicus. The tumor, which lay within the umbilicus, was roughly spherical and about 3 cm. in diameter. The surface was covered with blackish debris. The cut surface was roughly papillomatous. The epithelium over the projections was thin. The stroma was grayish white and was studded with fine yellowish nodules. At no point was the tumor attached to the peritoneum.

On microscopic examination a thin epidermis was seen to cover a rather edematous stroma. Embedded in this cellular (ectogenic) stroma were gland structures of two types: (1) the ordinary sweat gland, and (2) the rudimentary simple tubular glands lined with cylindric epithelium. The lumens contained debris (fig. 1). Under higher magnification many of these cylindric cells were seen to be ciliated. The blepharoplasts showed remarkably well. The simple tubular glands were morphologically indistinguishable from those of the endometrium. In scattered areas the cells were replaced by phagocytes containing vacuoles such as occur in blood cysts. This microscopic picture was comparable to that in the cases previously described.

DIAGNOSIS

Endometriosis always occurs during the years of ovarian activity. The cyclic nature of the symptoms, corresponding to the menstrual

periods, will usually suggest endometriosis. Any or all of the following symptoms may be present:

Secretion of blood-tinged fluid
Pain around or in the umbilicus
Tenderness
Swelling
Itching
Bluish discoloration

The tumors usually reach full size in from two to six months. Generally, they range from 1 to 3 cm. in diameter, occasionally reaching a diameter of 5 cm. Keene and Kimbrough pointed out the necessity for accurate differentiation of such tumors from uterine fistulas, which also may produce menstruation.

TREATMENT

The treatment of election is wide excision, and the technic is that used for ventral hernia. In addition, some authors, notably Baltzer, have recommended exploration of the peritoneal cavity for further foci. Roentgen and radium irradiation may be used during the menopausal period to inactivate the ovary. This treatment is recommended by Strongin in select cases. However, during the active sexual life of the woman operation is recommended unless there be some contra-indication.

CHRONOLOGIC REPORT

<i>Author</i>	<i>Year</i>
1. Villar	1886
2. Terrier	1887
3. Tourneux	1889
4. Wullstein	1893
5. Mintz	1899
6. Green	1899
7. Giannettasio	1900
8. Von Noorden.....	1901
9. Ehrlich	1909
10. Goddard	1909
11. Goddard	1909
12. Mintz	1909
13. Mintz	1909
14. Herzenberg	1909
15. Cullen	1912
16. Waegeler	1913
17. Zitronblatt	1913
18. Barker	1913

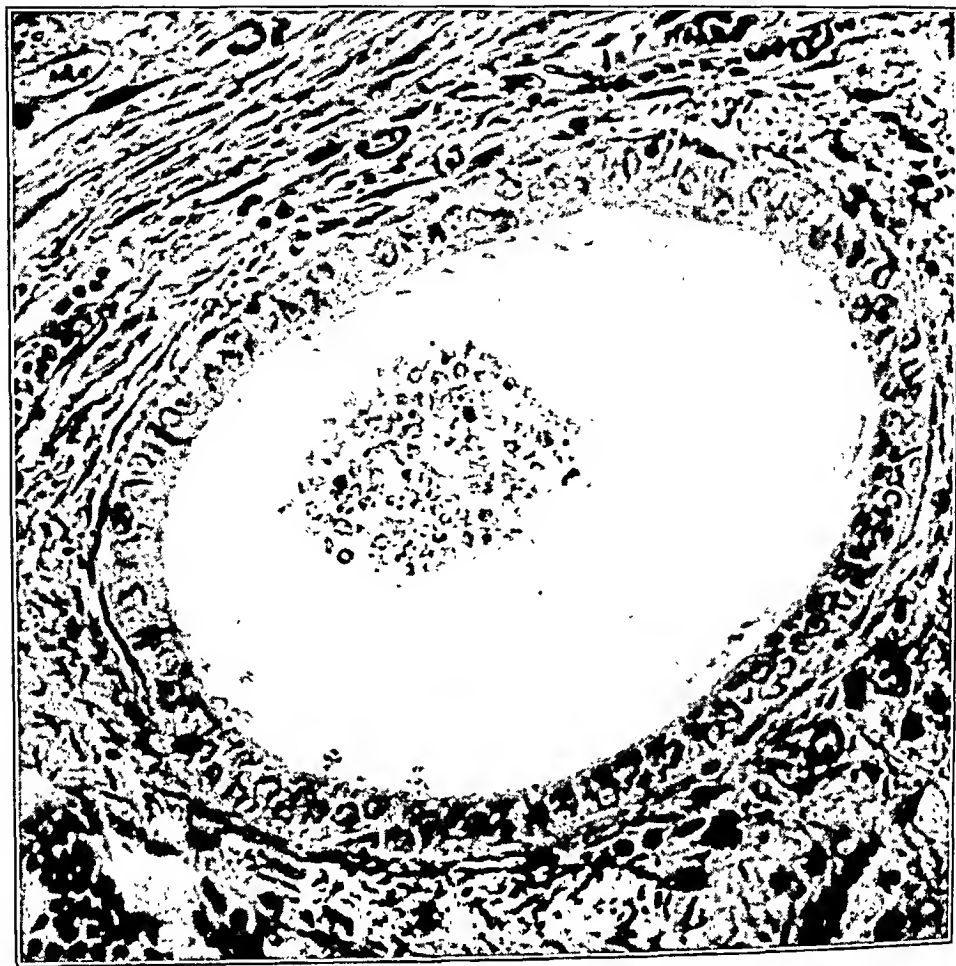


Fig. 1.—Simple tubular gland within the cellular stroma.



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17. Zitronblatt	1913
18. Barker	1913

	<i>Author</i>	<i>Year</i>
19.	Jones	1913
20.	Lindau	1914
21.	Lindau	1914
*22.	Ribbert	1914
23.	Rohdenberg	1919
24.	Mathias	1920
25.	Guthrie	1920
26.	Adams	1920
27.	Mahle and MacCarty.....	1920
28.	Keitler	1923
29.	Lauche	1923
30.	Lauche	1923
31.	Lauche	1923
32.	Tobler	1923
33.	Tobler	1923
34.	Andrews	1925
35.	Schiffmann and Seyfer.....	1925
36.	Edwards and Spencer.....	1925
37.	Stacy and associates.....	1926
38.	Walz	1926
39.	Anglesio	1926
40.	Weller	1927
41.	Weller	1927
42.	Oberling and Hickel.....	1927
43.	Steiner	1927
44.	Palmen	1927
45.	Palmen	1927
46.	Palmen	1927
*47.	Jacobsen	1927
48.	Lelièvre and Montpellier.....	1927
49.	Kohler	1927
50.	Foderl	1927
51.	Baltzer	1927
52.	Busser and associates.....	1928
53.	Roques	1928
54.	Baltzer	1929
55.	Frero	1929
56.	Holm	1930
57.	Holm	1930
58.	Butoma and Schereschewsky.....	1930
*59.	Tonkes	1930
60.	Enzer	1930

<i>Author</i>	<i>Year</i>
61. Keene and Kimbrough.....	1930
62. Keene and Kimbrough.....	1930
63. Spitz	1931
*64. Brown	1931
65. Habbe	1931
*66. Hanke	1931
67. Thompson	1931
*68. Adams-Ray	1932
*69. Adams-Ray	1932
*70. Adams-Ray	1932
*71. Adams-Ray	1932
*72. Adams-Ray	1932
*73. Adams-Ray	1932
*74. Adams-Ray	1932
75. Stetson and Moran.....	1932
76. Siedentopf	1932
77. Longwood	1932
78. Herberz	1933
79. Herberz	1933
80. Herberz	1933
81. Lanos and Busser.....	1933
*82. Bingham and Templeton.....	1934
*83. Galasso and associates.....	1934
*84. Schwarz	1934
*85. Harbitz	1934
*86. Harbitz	1934
*87. Harbitz	1934
*88. Harbitz	1934
*89. Planson	1934
*90. Knoflach	1935
*91. Marmol	1935
*92. Tølbøll	1935
*93. Strongin	1936
*94. Strongin	1936
*95. Strongin	1936
*96. Vanderzyphen and van Bogaert.....	1936
*97. Boggs	1937

* Not listed by previous authors.

SUMMARY

1. Tissues which are morphologically indistinguishable from the endometrium occur in the umbilicus.

2. The absence of the uterus is no bar to ovarian function.
3. A vicarious form of menstruation may take place after the removal of the uterus.
4. Endometriosis of the umbilicus is amenable to surgical treatment.
5. Ninety-seven cases of endometriosis of the umbilicus have been reported between 1886 and 1937.

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BIBLIOGRAPHY

- Adams, L., cited by Cullen, T. S.: Distribution of Adenomyomas Containing Uterine Mucosa, *Arch. Surg.* **1**:215 (Sept.) 1920.
- Adams-Ray, J.: On Extragenital and Inguinal Endometriosis and Its Surgical Importance, *Acta chir. Scandinav.* **70**:167, 1932.
- Andrews, H. R.: A Case of Endometrioma of the Umbilicus, *J. Obst. & Gynaec. Brit. Emp.* **32**:545, 1925.
- Anglesio, B.: Un caso di adenoma vero dell' ombelico, *Minerva med.* **6**:174, 1926.
- Baltzer, H.: Ueber heterope endometrioiden Wucherungen insbesondere am Nabel, *Zentralbl. f. Gynäk.* **53**:99, 1929.
- Ueber heterope endometrioiden Wucherungen, *Arch. f. klin. Chir.* **147**:555, 1927.
- Barker, A. E.: Three Cases of Solid Tumors of the Umbilicus in Adults, *Lancet* **2**:128, 1913.
- Bingham, E. M., and Templeton, W. K.: Umbilical Endometrioma, *California & West. Med.* **41**:330, 1934.
- Brown, R.: Endometrioma of the Umbilicus, *S. Clin. North America* **11**:931, 1931.
- Busser, F.; Van der Horst, and Drouhard: Endomètre de l'ombilic, *Ann. d'anat. path.* **5**:229, 1928.
- Butoma, V., and Schereschewsky, J. I.: Zur Frage über die menstruellen Veränderungen in extragenitalen Heterotopien, *Virchows Arch. f. path. Anat.* **274**:716, 1930.
- Cullen, T. S.: Umbilicus and Its Diseases, Philadelphia, W. B. Saunders Company, 1916, p. 373.
- Distribution of Adenomyomas Containing Uterine Mucosa, *Arch. Surg.* **1**:215 (Sept.) 1920.
- Edwards, C. R., and Spencer, H. R.: Adenomyoma of the Umbilicus, *Arch. Surg.* **11**:684 (Nov.) 1925.
- Ehrlich, H.: Primäres doppelseitiges Mammarcarcinom und wahres Nabeladenom, *Arch. f. klin. Chir.* **89**:742, 1909.
- Enzer, N.: Endometriomyoma of the Umbilicus, *Arch. Path.* **10**:879 (Dec.) 1930.
- Foderl, V.: Ein echtes Nabeladenom, *Beitr. z. klin. Chir.* **138**:255, 1926.
- Frero, A. J.: Endometriosis del ombligo, *Bol. Soc. de obst. y ginec.* **8**:516, 1929.
- Galasso, A.; Sherman, B. J., and Burns, V. E.: Endometriosis of Umbilicus, *J. A. M. A.* **102**:1845 (June 2) 1934.
- Giannettasio, N.: Sur les tumeurs de l'ombilic, *Arch. gén. de méd., Paris* **3**:52, 1900.
- Goddard, S. W.: Two Umbilical Tumours of Probable Uterine Origin, *Surg., Gynec. & Obst.* **9**:249, 1909.
- Green, C. D.: A Case of Umbilical Papilloma, *Tr. Path. Soc., London* **50**:243, 1899.

- Guthrie, D., cited by Cullen (1920).
- Habbe, K.: Ueber einen Fall von endometrioider Wucherung am Nabel mit Schweissdrüsenwucherung, mit Betrachtungen über die Genese, *Zentralbl. f. Gynäk.* **22**:917, 1931.
- Hanke, H.: Ueber Endometriose des Nabels, *Arch. f. klin. Chir.* **166**:192, 1931.
- Harbitz, H. F.: Clinical, Pathogenetic and Experimental Investigations of Endometriosis, *Acta chir. Scandinav. (supp. 30)* **74**:1, 1934.
- Herberz, O.: Zur Kasuistik der Nabelendometriosen, *Monatschr. f. Geburtsh. u. Gynäk.* **95**:259, 1933.
- Herzenberg, R.: Ein Beitrag zum wahren Adenom des Nabels, *Deutsche med. Wchnschr.* **1**:889, 1909.
- Holm, E.: Fibroadenoma metastaticum malignum og nogle bemerkninger om det aegte umbilicaladenom, *Bibliot. f. læger* **122**:197, 1930.
- Jacobsen, V. C.: Ectopic Endometriosis, *Am. J. Path.* **3**:554, 1927.
- Jones, E. G., cited by Cullen (1916).
- Keene, F. E., and Kimbrough, R. A.: Endometriosis, *J. A. M. A.* **95**:1164 (Oct. 18) 1930.
- Keitler, H.: Ueber einen Fall von Nabeladenom mit Bemerkungen über vikariierende Menstruation, *Monatschr. f. Geburtsh. u. Gynäk.* **64**:171, 1923.
- Knoflach, J. G.: Endometriosis der Leistengegend und des Nabels bei einer Patientin, *Wien. klin. Wchnschr.* **48**:698, 1935.
- Kohler, R.: Adenomyosis des Nabels, *Zentralbl. f. Gynäk.* **51**:2201, 1927.
- Lanos, J., and Busser, F.: Sur un cas d'endométrisme de l'ombilic, *Bull. et mém. Soc. d. chirurgiens de Paris* **25**:134, 1933.
- Lauche, A.: Die extragenitalen heterotopen Epithelwucherungen von Bau der Uterusschleimhaut, *Virchows Arch. f. path. Anat.* **243**:298, 1923.
- Lelièvre and Montpellier: Sur un cas d'endométrisme de la région ombilicale, *Bull. Assoc. franç. p. l'étude du cancer* **16**:867, 1927.
- Lindau, G. H.: Ein Beitrag zur Kenntnis des wahren Nabeladenoms, *Stud. z. Path. d. Entwcklg.* **1**:375, 1914.
- Longwood, O. W.: Endometroid Heteropias of the Umbilicus, *Am. J. Obst. & Gynec.* **23**:582, 1932.
- Mahle, A. E., and MacCarty, W. C.: Ectopic Adenomyoma of Uterine Type, *J. Lab. & Clin. Med.* **5**:218, 1920.
- Marmol, D. G.: Endometriosis, *Rev. méd. cubana* **46**:385, 1935.
- Mathias, E.: Zur Kasuistik seltener Geschwulstbildungen: Chorioblastom des Nabels, *Berl. klin. Wchnschr.* **17**:398, 1920.
- Mintz, W.: Das Nabeladenom, *Arch. f. klin. Chir.* **89**:385, 1909.
- Das wahre Adenom des Nabels, *Deutsche Ztschr. f. Chir.* **51**:545, 1899.
- von Noorden, W.: Ein Schweissdrüsenadenom mit Sitz im Nabel und ein Beitrag zu den Nabelgeschwülsten, *Deutsche Ztschr. f. Chir.* **59**:215, 1901.
- Oberling, C., and Hickel, P.: Le problème de l'endométrisme, *Bull. Assoc. franç. p. l'étude du cancer* **16**:691, 1927.
- Palmen, A. J.: Zur Kenntnis der Nabeladenome, *Acta chir. Scandinav.* **62**:310, 1927.
- Planson, V.: Endométrisme de la région ombilicale, *Bull. et mém. Soc. d. chirurgiens de Paris* **26**:611, 1934.
- Ribbert, H.: *Geschwulstlehre für Aerzte und Studierende*, ed. 2, Bonn, F. Cohen, 1914.

- Rohdenburg, G. L.: Fibroadenoma of the Umbilicus, *Proc. New York Path. Soc.* **19:2**, 1919.
- Roques, F.: Endometrial Tumour of the Umbilicus, *Proc. Roy. Soc. Med.* **21:538**, 1928.
- Sampson, J. A.: Benign and Malignant Endometrial Implants, *Surg., Gynec. & Obst.* **38:287**, 1924.
- Schiffmann, J., and Seyfert, W.: Ein Nabeladenom, *Arch. f. Gynäk.* **87:208**, 1925.
- Schwarz, T.: Umbilical Endometriosis with Involvement of Adnexa, *Bratisl. lekár. listy* **14:19**, 1934.
- Siedentopf, H.: Ein Fall von Nabel-Endometriose, *Zentralbl. f. Gynäk.* **56:2323**, 1932.
- Spitz, H.: Adenomyoma of the Umbilicus, *Am. J. Clin. Path.* **2:155**, 1932.
- Stacy, L. J.; Drips, D. G.; Offut, S. R., and Moench, L. M.: Adenomyoma of the Umbilicus, *M. Clin. North America* **10:671**, 1926.
- Steiner, H.: Ein Nabeladenom, *Zentralbl. f. Gynäk.* **51:2796**, 1927.
- Stetson, H. G., and Moran, J. E.: Endometriosis, *New England J. Med.* **206:52**, 1932.
- Strongin, H. F.: Endometriosis of Umbilicus, *Am. J. Obst. & Gynec.* **32:336**, 1936.
- Terrier, F.: Tumeur verruqueuse (papillome) de l'ombilic chez une femme, *Bull. et mém. Soc. d. chirurgiens de Paris* **13:422**, 1887.
- Thompson, W. McL.: Report of a Case of Endometriosis of the Umbilicus, *Am. J. Obst. & Gynec.* **22:917**, 1931.
- Tobler, T.: Ueber tumorartige entzündliche uterindrüsenähnliche Wucherungen des Peritonealepithels in Laparotomienarben und über ebensolche Spontanwucherungen im Nabel, *Frankfurt. Ztschr. f. Path.* **29:558**, 1923.
- Tølbøll, E.: Endometriosis, *Hospitaltid.* **78:963**, 1935.
- Tonkes, E.: Menstrual Cycle in Ectopic Endometrium, *Nederl. tijdschr. v. verlosk. en gynaec.* **34:79**, 1930.
- Tourneux, F.: Sur la presence de cellules epitheliales ciliées dans une tumeur de l'ombilic chez l'adulte, *Compt. rend. Soc. de biol.* **41:200**, 1889.
- Vanderzypen and van Bogaert, C.: Endométriosis, *Bruxelles-méd.* **16:1190**, 1936.
- Villar, F.: Tumeurs de l'ombilic, *Thesis, Paris*, no. 19, Paris, A. Davy, 1886, p. 71.
- Waegeler, H.: Zur Histogenese der Nabeladenome nebst einem kasuistischen Beitrag, *Frankfurt. Ztschr. f. Path.* **14:367**, 1913.
- Walz, K.: Zur Frage der Entstehung der heterotopen Wucherungen vom Bau der Uterusschleimhaut, *Centralbl. f. allg. Path. u. path. Anat.* **37:290**, 1926.
- Weller, C. V.: Endometriosis of the Umbilicus, *Am. J. Path.* **3:553**, 1937. .
- Endometriosis of the Umbilicus, *ibid.* **11:281**, 1935.
- Wullstein, L.: Eine Geschwulst des Nabels (Kombination von Cystadenom der Schweissdrüsen mit cavernösem Angiom), *Arb. a. d. path. Inst. in Göttingen*, 1893, pp. 245-253.
- Eine Geschwulst der Brustdrüse eines Kindes (congenitales Angioma simplex hyperplasticum), *ibid.*, 1893, pp. 253-257.
- Zitronblatt, A.: Zur Kasuistik und Histogenese der Nabeladenome, *Deutsche med. Wchnschr.* **39:371**, 1913.

VAGINAL HERNIA

WITH A REVIEW OF THE LITERATURE

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Vaginal hernia is a herniation of the peritoneum pushing downward through the pelvic floor into the vaginal vault or along the wall between the vagina and the rectum or bladder, sometimes extending between them all the way to the perineum. With prolapsus uteri, it is not uncommon; but uncomplicated vaginal hernia is considered rare. The condition is interesting to obstetricians, as it appears to occur most frequently during or following labor; it is of interest also to gynecologists, in the differential diagnosis of cystocele and rectocele and as a complication of prolapsus uteri.

Vaginal hernia is a term used to designate a subvariety of pelvic hernia, the latter term including all hernias through the pelvic floor. This subvariety of hernia is named from the point of egress, the practice used in the nomenclature of the inguinal hernias. The recognition and use of this term would group instances of this rare type of hernia together under one main heading for the purpose of indexing histories and medical literature. It would also be consistent with the best usage in nomenclature of hernia, bringing the designation of these cases into harmony with the terminology of hernias in general, which is according to the point of origin and not of termination. The *Quarterly Cumulative Index Medicus* lists instances of this type of hernia separately, using the term vaginal instead of cul-de-sac, with a separate listing for perineal, etc. Few textbooks adequately describe this condition, but the article by D. G. Ward in Kelly's "Gynecology" is complete and well illustrated.

The first case of vaginal hernia was reported by Garengot in "The Memoirs of the Royal Academy of Surgery," early in the sixteenth century. The condition occurred in a woman one month after a fifth confinement, when she attempted to lift a heavy weight. In 1804, Sir Astley Cooper, under the title "Abdominal Hernia," reported 3 cases of pelvic hernia without complications. He expressed surprise that more cases were not encountered in history and stated that the oblique direction of the pelvis is a factor in the prevention of this type of hernia. Barker in 1876 found enough cases to allow a satisfactory anatomic

classification and listed the causes of the condition as (1) violent shock from falls, (2) strong physical efforts and (3) difficult parturition. The first operation for vaginal hernia, apparently caused by large fibroids, was performed in 1885.

CLASSIFICATION

This classification of pelvic hernias follows that of Barker:

1. Vaginal—(a) Anterior—passing between the bladder and the cervix.
 - (b) Posterior—passing posterior to the uterus and involving the bulk of the vaginal and the recto-vaginal pouch.
 - (c) Postoperative (Postoperative vaginal hernia is actually in a third subdivision by itself, a classification used by Masson).
2. Perineal—passing through the rectal vaginal pouch, leaving the vault of the vagina normal.
3. Pudendal—dissecting the side of the pelvis and appearing in the labia majora.
4. Complete pelvic (Complete pelvic hernia consists of the extrusion of all the pelvic contents and is not a true vaginal hernia).
5. An additional type added by Zuckerkandel, namely, a protrusion of the cul-de-sac into the anterior wall and lumen of the rectum.

These hernias all have a separate peritoneal sac, which cystocele and rectocele do not have, and a definite ring, which is absent in prolapsus uteri. As such, cystocele and rectocele and prolapsus uteri with pelvic floor are to be classed as false vaginal hernias.

REVIEW OF THE LITERATURE

A marked confusion of terms and an inadequacy of description make it almost impossible to review the literature accurately, particularly from the standpoint of identification of a true vaginal hernia from the descriptions of many authors. Analysis frequently proves that the vaginal bulging or mass is the result of a prolapsus or descensus of the uterus accompanied by bulging of abdominal contents.

The first reported case was that of Garengéot, in the sixteenth century, followed by 3 of Cooper. Smellie later reported 3 cases, followed by Sweepster in 1919. Moschcowitz in 1912 reported 25 cases in the literature with 1 of his own of the perineal variety. Chase in 1922 was able to identify only 13 cases, including 1 of his own. Miles in a careful summary of the literature in 1926 was able to find only 9 cases of definite vaginal hernia, of which 3 were observed without operation or

autopsy. To these he added 2 of his own. Three of Barker's cases reported in 1876 were studied by Miles, and only 1 was accepted as an instance of true vaginal hernia. Miles' 11 cases are as follows:

Case 1: Taylor in 1831 reported the case of a 22 year old woman in her second pregnancy. Three days post partum a vaginal mass was noted; it was large at the end of thirteen months, occupying a posterior commissure of the labia below the external surfaces. The diagnosis was postvaginal midline vaginal hernia.

Case 2: Etheridge in 1887 reported the case of a woman aged 19 or 20. During her sixth month of pregnancy, the patient was jumping a rope and felt something come down through the vagina. Delivery was normal. After delivery, a mass was noted, appearing with lifting and straining, coming out between the thighs. Examination showed a large opening in the roof of the vagina with edges forming a definite ring. This opening was to the left of the uterus, anterior to the broad ligament and posterior to the bladder. The hernia extended into the vagina and was not lateral to the vaginal canal, a feature which differentiated it from a pudendal hernia. This was of anterior vaginal type.

Case 3: Barker in 1876 reported the case of a 32 year old woman who fell during her first pregnancy. She soon felt a mass protruding in the vagina. The symptoms were those of strangulation of a loop of intestine. A definite ring was felt in the vaginal vault, posterior to the cervix and just to the right of the midline, $1\frac{1}{2}$ inches (4 cm.) in diameter. The hernia was easily reduced. It was followed by eight successive attacks.

Case 4: Birehenall in 1869 reported the case of a 53 year old woman who died eighteen hours after an intra-abdominal injury. The only autopsy performed in a case of vaginal hernia was made in this case. The patient had long suffered from a vaginal hernia. The autopsy showed a small point of perforation of the intestine.

Case 5: Thomas in 1885 performed the first operation for vaginal hernia, on a multipara aged 39. The vaginal mass had been present for six years, extending to the middle of the thigh. Pain appeared in the bladder and rectum with reduction. The pelvic organs were in normal positions. The hernial orifice was in the vaginal fornix, through an opening in the broad ligament. At operation the sac was reduced by the insertion of an assistant's hand in the vagina and sewed to the anterior abdominal incision. Excellent results followed. Thomas reported 4 cases also of posterior midline vaginal hernia, in which operation produced cures.

Case 6: Huginer in 1912 reported an operation, performed in 1911, for prolapse of the uterus with vaginal prolapse and attendant disorders. The operation consisted of amputation of the cervix, anterior colporrhaphy, perineorrhaphy, and abdominal hysteropexy. In six months the mass recurred, diagnosed as rectocele. At operation, the sac of a definite vaginal hernia of the eul-de-sac was encountered.

Case 7: Lathrop in 1913 reported the case of a multipara aged 41. In July 1908, an operation was performed for cystocele, rectocele and prolapsus uteri, with abdominal fixations. In December 1908, the rectocele recurred and operation was done, followed by a second protrusion. In 1909, the patient had a delivery, followed by an increase in the size of the mass. In 1912, an operation showed this to be a vaginal hernia. Broad ligament and uterus were used to close the defect.

Case 8: Hartmann in 1916-1917 reported the case of a 30 year old woman who had had her first child at the age of 22 and her second at the age of 24.

After the second birth she experienced prolapse of the uterus, which was treated by abdominal fixation. The birth of a third child, when she was 29, was followed by a prolapsing vaginal mass. No rectocele or prolapsing uterus was encountered in this mass. A subsequent pregnancy was followed by an operation and permanent cure of the vaginal hernia.

Case 9: Sweetser in 1919 reported the case of a single woman aged 21, who had experienced no pregnancy. She had had a pyosalpinx with fever for five years followed by a swelling in the vagina. A definite vaginal hernial ring was encountered, while the perineum and the uterus were intact. At operation, the levators were sutured.

Case 10: Miles in 1926 reported the case of a 46 year old woman, with three children. Seventeen years after the birth of the last child, an abdominal swelling was encountered. Examination showed a bulging of the rectum in the vagina, thought to be a rectocele. At operation, much fluid and a multilocular cystadenoma of the ovary were encountered. The uterus was high. The pelvis was not explored. A second operation, twenty-six days later, disclosed a water-filled cyst connecting with the abdomen through a small opening at the level of the posterior cervix and between the vagina and the rectum.

Case 11: Miles in 1920 reported the case of a 35 year old woman with five children. Abdominal distention of two years' duration was found to be due to an excess of fluid and a multilocular cystadenoma of the ovary. The uterus was high. A mass was found in the posterior vagina. No rectocele was present. The cul-de-sac was large, with the opening extending down between the rectum and the vagina.

Hundley, in 1927, outlined a variation of surgical repair based on experience in 4 cases. His procedure, which he recommended for use only for patients who have passed the menopause, consists of exposing the uterovesical peritoneum and drawing the fundus sharply forward into the opening. The apex of the invaginated vaginal hernial pouch is then pushed by the index finger along the posterior surface of the uterus into the opening above and firmly anchored by two linen sutures which pass through the entire cul-de-sac, peritoneum, pelvic fascia and vaginal mucous membrane. Thus a vagina of normal length is retained. The cervix is subsequently amputated.

Crossen in 1930 reported 2 cases:

Case 1: An operation for uterine prolapse on a patient 66 years of age was followed within four years by a characteristic hernia of the cul-de-sac. Because of a bad heart and adiposity the hernial repair was performed under local anesthetic.

Case 2: The patient was 69 years of age, a poor operative risk. Pessaries and similar appliances never failed to maintain the bladder and uterus in place, but a posterior vaginal mass slipped out past the pessary. At operation, the uterine prolapse was treated by vaginal shortening of the broad ligament, while the hernia of the cul-de-sac was treated by repair of the pelvic floor.

Green in 1931, reviewing the literature, stated that of 50 or 60 cases reported, between 10 and 12 were of the true vaginal type, with an equal number of the perineal type. He reported 2 cases:

Case 1: The patient was 62 years of age and had experienced five labors. At the age of 32 she had had her first labor, which had been prolonged until

delivery by means of forceps became necessary. It was followed by a vaginal bulging. After the patient had at first refused an operation, one was performed in 1929. At this time, a large posterior vaginal hernia was encountered, filled with intestines. It was repaired by suture of the levator muscels.

Case 2: The patient was a 62 year old woman, with five children. At 22 years of age she had been delivered by a midwife, with forceps. At 29 she had had a large hernia, occupying the entire vagina, easily reduced; it was found to contain intestines. No cystocele or rectocele was present, and the pelvic organs were in normal positions.

Williamson in 1932 reported 2 cases:

Case 1: A negress, age 46, a unipara, was operated on in 1926 for complete uterine prolapse, with lacerations of the pelvic floor. The hysterectomy was followed by perineal breakdown and complete prolapse of the vagina. This was treated by sewing the vaginal vault to the fascia of the lower anterior abdominal wall. The results were good. This case hardly warrants the diagnosis of true vaginal hernia.

Case 2: A white woman, age 48, suffered from an abdominal mass for five years. There was a protrusion of the posterior vaginal vault through the vaginal orifice. At operation, no serosa of the cul-de-sac was encountered, but the mass was found to be inflammatory in consistency, constituting a huge hydrosalpinx and cystic ovary. A subtotal hysterectomy and bilateral salpingo-oophorectomy were performed and the cul-de-sac closed by approximating the uterosacral ligament. The cervical stump was supported by the round ligaments and the denuded areas of the pelvic floor covered by peritoneal flaps. Results were satisfactory.

Masson encountered his first case in 1926, at an operation supposedly for rectocele. Since then, there have been 11 cases at the Mayo clinic according to his last report in 1932. His first 5 cases, reported in 1928, are as follows:

Case 1: Multiple fibromyomas of the uterus associated with hernia of the cul-de-sac occurred in a 44 year old woman who had experienced four pregnancies. There was no postoperative recurrence of hernia.

Case 2: A woman 42 years old who had been pregnant five times, was examined in 1919. In 1917, a perineorrhaphy for a supposed rectocele was performed followed by a prompt recurrence of symptoms. In six months uterine suspension and a second perineorrhaphy were performed, and again the symptoms promptly recurred. Since then, attacks of abdominal pain and distention had become more severe and were associated with vomiting. The hernia was of posterior vaginal type.

Case 3: A woman 65 years old, who had been pregnant ten times, had suffered from a vaginal mass for five years. Supports were useless and irritating. The vaginal mass consisted of the uterus in addition to a hernial sac. Herniorrhaphy was performed three weeks after uterine suspension.

Case 4: A woman, 39, with two children, aged 8 and 10 years, was submitted to uterine anterior fixation for supposed prolapse, after her last pregnancy. The condition promptly recurred when she stood up. A protruding vaginal mass was present at examination, which showed complete uterine prolapse, as well as cystocele. At operation, the rectum was isolated from the mass, and a vaginal hernia separate from the prolapse was encountered.

Case 5: The patient, a 57 year old woman, had three children. After the birth of the last, in 1904, she was troubled by a vaginal mass on standing or straining. In 1906 a perineorrhaphy and uterine suspension were performed, followed by prompt recurrence. In 1913 a Kocher operation for prolapse was performed and was followed suddenly in three months by a recurrence. At operation, no cystocele, but a large posterior vaginal hernia, was encountered.

Erdman in 1932 cited a case reported by Michelson and Lukin in which a vaginal hernia was mistaken for a vaginal polyp and excised with fatal results.

Bueermann in 1932 reported 3 cases:

Case 1: A 61 year old woman, who had been pregnant three times suffered from a posterior vaginal mass of fifteen years' duration. Gurgling sounds were noted when the patient walked. A subtotal hysterectomy had been performed in 1912, five years before the mass was noted. In 1913, a rectocele was repaired, and the condition immediately recurred. In 1914, an unsuccessful attempt at repair was made. The patient was told her tissues were too weak for further repair. The mass was easily reduced and recurred with coughing or strain. Gurgling and peristalsis were noted. No cystocele or rectocele was found on examination. The mass was a large vaginal hernia.

Case 2: A 67 year old nullipara complained of rectal and vaginal pressure. In 1928 a posterior vaginal mass was found. A perineorrhaphy and colporrhaphy gave relief of short duration. No uterine prolapse was present. The posterior vaginal wall was redundant. A diagnosis of vaginal hernia was made at operation. In 1931 a rectal hernia was discovered.

Case 3: A 66 year old woman, with six children, complained of a vaginal mass of six months' duration, which appeared with cough or strain and disappeared when she lay down. She had no backaches. A bearing-down sensation was noted with micturition. The frequency of occurrence was greater in the daytime. The mass was in the anterior part of the vagina. There was no cystocele, according to the sound in the bladder.

Dew in 1934 reported 2 cases:

Case 1: A woman 56 years of age suffered from cirrhosis of the liver, associated with ascites. In 1925 a vaginal hernia was encountered. Her five pregnancies had all been easy. At operation, a large rectocele was encountered below the posterior hernia. Operation was followed by death.

Case 2: A 38 year old woman had had four pregnancies, of which the first had terminated in a face presentation with five days' labor. Three years previously, some heavy lifting had been followed by severe pains in the lower part of the back. A pessary did not give satisfaction. A vaginal mass appeared, associated with constipation and difficulty in defecation. At operation, a posterior vaginal hernia was encountered measuring 6 by 8 cm., lined with peritoneum, associated with diastasis of the levators.

Black in 1934 reported the following case:

A 65 year old septipara, with children between the ages of 37 and 21, had fallen seven weeks before examination. After the fall, a large mass had appeared, with a second degree laceration of the perineum. No uterine prolapse was

encountered. After a diagnosis of vaginal hernia, a high perineorrhaphy was performed. The sac was filled with small intestines and located in the midline. The neck of the sac admitted an index finger.

Caillot and his associates in 1935 reported a case of perforation of the cul-de-sac by curet and escape of the sigmoid colon through the orifice thus produced. Total abdominal hysterectomy was performed. The presence of a true vaginal hernia is to be doubted. Cervenansky reported a case of pelvic hernia of perineal type in February 1936, but the last case, one of a lateral hernia of the cul-de-sac, was reported by de Modena in December 1936.

Stearns, in January 1936, reported the last true cases of vaginal hernia:

Case 1: The patient was a tripara, aged 53, who had had normal labors. Fibrillating heart and mitral stenosis were complications, associated with marked ascites, which served as a contributing factor in the production of a vaginal mass of eighteen months' duration. The diagnosis on examination was rectocele and prolapse of the uterus. This mass was extruded only on straining and was preceded by a large cervix. The operation showed the condition to be a combined prolapse and vaginal hernia. The hernial sac was empty. The condition was followed in three months by embolism. The pelvis and adjacent organs were not examined at autopsy.

Case 2: A quintipara, 56 years old, whose first pregnancy had been sixteen years previously, had suffered from a dragging-down sensation in the pelvis for three years. A 5 foot fall seven years ago was followed by a vaginal bulging. This disappeared when she lay down. Retention of urine was difficult. The diagnosis on three previous incomplete examinations had been cystocele and rectocele, and in one case prolapse of the uterus. A thorough examination showed no cystocele, rectocele or prolapse. The report is indefinite as to whether the vaginal hernia was of the anterior or the posterior type.

REPORT OF A CASE

The present case is interesting because for the first time microscopic examination was made of tissues of the pelvic structure and pathologic changes were observed which are important particularly in the development of hernia in older patients.

A white woman, age 72, who had had three children with normal deliveries, entered the hospital because of a bulging mass in the vagina and disease of the bladder. Nine years previously the patient was operated on for cystocele, and the cervix was amputated. At that time, the perineum was slightly lacerated but was not repaired. About a year later, the patient noticed a bulging mass coming from the vagina, which gradually increased in size, and caused considerable trouble, creating distress when her bowels moved. It was as if everything were dropping out. When she was on her feet, the mass protruded from the vagina, appeared filled with fluid and "crunched" when she walked about. She never wore a support or pessary. At times she was troubled with frequency of urination and noticed a burning sensation. Her appetite was good, and she was not constipated as a rule. Physical examination showed her to be in fairly excellent

condition. The pulse rate was slow, with a dropped beat of one in three. The blood pressure was 190 systolic and 100 diastolic. There was no tenderness or mass in the abdomen. A bulging mass was pouching out the posterior vagina and coming out the vulva. When pushed inward, this seemed to come from immediately behind the cervix. Prior to operation, her blood pressure dropped to 140 systolic and 60 diastolic.

With the patient under ether anesthesia, the posterior vaginal mucosa was divided in the midline from the perineum up to the cervix. The hernial sac, which had pushed out of the vagina, was dissected free and ligated high at the neck above the hernial ring, which was found to be in the posterior fornix immediately posterior to the cervix. The neck was then sutured to the posterior side of the cervix, the elevators of the rectum brought over the rectum, the vaginal mucous membrane closed and a perineorrhaphy performed. This shortened the vagina considerably, but there was some posterior floor to the vagina. The bladder was in the normal position. Examination one year later showed no recurrence.

Histologic Examination.—Redundant tissue encountered at the time of the vaginal repair, together with specimens of the hernial sac and some tissue from the floor about the neck of the hernial sac, was removed for microscopic examination. Sections taken near the surface revealed stratified squamous epithelium, apparently in a healthy condition, with some areas showing increased thickness and a tendency toward a layer of keratin on the surface such as is noted in vaginal prolapse. Invading the basal layer from the lamina propria were a few wandering cells of the lymphocytic type, among which plasma cells could be identified. Swelling, edema and vacuolation occurred in the non-keratin-forming parts of the epithelium. Smooth muscle fibers below the lamina propria came in small bundles or even isolated as single atrophic fibers, usually buried in an overwhelming proliferation of fibrocollagenous tissue, which in areas exhibited highly cellular inflammatory scar reaction. Over considerable areas the muscle and the elastic tissue were completely lost and overwhelmed by scarring, which ultimately exhibited diffuse hyalinization and a definite degeneration, which actually became granular in character. The same change was encountered in the fibro-tendinous tissue of the pelvic floor about the hernial neck.

Blood vessels appear as finely compressed channels and were uncommon except in the areas of better preserved smooth muscle in which arterioles exhibited marked hyalocollagenous thickening of the intima, resembling senile obliterative endarteritis and commonly involving occlusion of the lumen. Near this region were elements of cervical tissue, including cervical glands, several of them cystic. This vascular change associated with alteration in the character of the normal vaginopelvic tissue had resulted in definite scarring and degeneration. The mechanism and change were identical with those in aneurysm of a vessel.

The pathologic diagnosis were senile arteriosclerosis of the vagina and the pelvis, endarteritis obliterans of the vagina and the pelvis and degenerative cellulitis of the vagina and the pelvis of vascular origin.

ANATOMY OF VAGINAL HERNIA

Vaginal hernia originates most frequently in the bottom of the cul-de-sac, the internal ring formed by the uterosacral ligaments and the anterior rectal wall, or by separated fibers of the pelvic fascia and levator ani muscle and the cervix. It appears in the vagina and vulva or protrudes through at the posterior commissure. This hernial protrusion



Above, a central zone of degenerating granular hyaline scarlike tissue, containing arterioles showing collapse and obliterative changes is located between more normal fibromuscular pelvic tissue ($\times 100$). Below, fibromuscular pelvic tissue undergoing granular change and dissolution, associated with traumatic hemorrhage, is located between two small arteries, *A*, showing complete senile hyaline obliterative endarteritis ($\times 100$).

occurs through a defect in the pelvic floor, which consists of a peritoneal surface, the levator ani muscles, a median anococcygeal raphe and the pelvic fascia. These are interrupted in their perfect closure of the pelvic outlet by the rectum, the vagina and the urethra. Posterior to the cervix their fusion along the line of the raphe is usually dense. Symington found the floor of the pelvis in the median plane to be about 2.5 cm. in thickness, composed of muscle and fascia. Derby, however, found the levator ani muscle to be the most variable muscle in the body, commonly affected by congenital weakness or absence of its intercommunicating fibers, and as such a prominent predisposing factor in formation of a hernia. The pelvic fascia which overlies the levator ani muscle passes from the brim of the true pelvis downward and inward to the bladder, with which it is intimately connected, and to the vagina, which it splits to enclose, united with the fascia of the opposite side, and is attached to the cervix uteri, where it helps to form the vaginal vault. This forms a fibrous sling which is the main support of the bladder and the strongest of the uterine supports. The posterior part of the fascia is deeper than the anterior and passes downward and inward to the rectal wall, to which it is intimately attached as part of the floor of the cul-de-sac. Posterior to the rectum it covers the piriformis muscle and is continuous above with the lamella of the lumbar fascia. The tendency toward a weakness of the midline structures posterior to the cervix is more easily understood on consideration of the embryologic formation of the pelvis and fascia as first described by Zuckerkandel in 1891. Breisky found the cul-de-sac in a 3 month female fetus to extend to a point where the uterovaginal canal still empties into the urethra. Ziegenspeck found the cul-de-sac to extend to the levator ani muscle in 2 of 56 specimens examined.

CAUSATION

Etiologically, vaginal hernia is based on anatomic, or most essentially traumatic, embryologic and pathologic change in the tissue. It is evident that in the absence of direct traumatic violence, such as may occur in labor, or of true pathologic changes in the tissue of the pelvic floor of inflammatory or degenerative type, the underlying source of herniation is a congenital defect or weakness in that floor. The uterosacral ligaments are totally incapable of preventing a tendency toward true vaginal hernia, and their weakening only induces prolapse. It has been found that Douglas' pouch extends down to the levator ani muscle in the fetus and at birth is already retracting and elevating, so that by puberty it has reached the level of the second and the third sacral vertebra. Failure of this change to take place leaves a weak space in the pelvic fascia just in front of the rectum, where the rectum passes through the pelvic floor, and accounts for the occurrence of

enterocele in young nulliparas. Another cause is the failure of the muscles of the pelvic floor, particularly the levator ani, which is a highly variable muscle in thickness and position, to give proper support to the pelvic fascia.

Trauma is a major contributing factor in the production of vaginal hernia. Labor itself could not cause this defect, but a large head with impaction and tearing of a firm vaginal wall or of the supporting pelvic floor with abrupt labor or instrumentation may produce it. The relaxation of muscles, tendons and fascia concomitant to pregnancy may easily lead to rupture. In 59.9 per cent of the reported cases the condition was noted in women who had experienced multiple pregnancies, which also serve to loosen the connective tissue attaching the uterus, the vagina and the pelvic floor. Greatly increased intra-abdominal pressure, such as occurs with obesity, ascites, intra-abdominal tumors and the like, or a sudden fall also leads to the formation of hernia.

Age, to a degree, is important. Buecrmann's statistics on 76 cases, in 48 of which age was mentioned, indicate the close connection between the period of productivity, particularly of multiparous pregnancies, and vaginal hernia. To this is added the recognized laxity and weakness of supportive structures in old age, the major source of which must be the vascular changes and alterations in the tissue described in the case here reported and noted below. Bueermann's list showed:

Years	No. of Cases
10-19	1
20-29	8
30-39	13
40-49	12
50-59	6
60-69	8

There has been little study of the pathologic changes in the pelvic floor. In 2 reported cases inflammatory changes, originating in pelvic inflammatory disease, were apparent causes of hernia. One factor which has not been studied is presented in my case report and indicates the importance of vascular changes in production of degenerative defects of the tissue. The resultant alteration resembles aneurysm and leads to an aneurysmal defect and breaking down of the supporting structure. This evidently must play a prominent part in cases of senile or arteriosclerotic conditions and in those in which the patient is nulliparous when trauma and congenital defects do not immediately explain the herniation.

In the normal or obliterated cul-de-sac, intestinal and intra-abdominal pressure is applied to the symphysis pubis and the bladder. But with the deepening of the cul-de-sac by whatever cause, this pressure falls

on the anterior and posterior vaginal wall and is deflected from the pelvic fascia, gradually causing a deepening and elongation of the pouch, which then extends down along the vaginal wall or protrudes into the vagina itself.

DIAGNOSIS

The failure to recognize this condition when it is a complicating factor in uterine prolapse may result in great disappointment from the operation for prolapse. The patient returns after a time, complaining of return of the prolapse, and examination shows a projecting mass. Bueermann showed that in 40.6 per cent of cases diagnosis was not made at first examination or at operation and the uterus had been removed prior to the onset of symptoms in 4 of 59 cases. Vaginal hernia must be differentiated from abscess, cyst, hematoma, lipoma, polyp, fibroma, prolapse of the uterus, vagina or rectum and cysts of Gartner's duct in the upper vagina, especially if connected with cysts of the parovarium. One should note carefully if the masses are reducible and have a hernial ring at the base.

In operation, greatest care should be exercised in upper vaginal swellings. With careful mucosal dissection, the hernial sac becomes exposed on elevation of the flaps. Caillot and his associates reported a case in which one such mass was mistaken for a uterus and perforated with a curet. Michelson and Lukin cited a case in which the amputation of a hernial mass which was interpreted as a polyp resulted in death.

Most masses in the upper part of the vagina are first considered rectoceles. However, one should note that the hernia appears when the patient stands, coughs or strains, disappears when she is in a recumbent position, has a definite hernial ring, gurgles on manual replacement of the bowel and has no connection with the rectum, as indicated by digital examination of the lumen and wall of the latter, although it may be simultaneously accompanied by rectocele, cystocele, prolapsing uterus or all of these conditions. Cystoscopic examination and discernment of sounds differentiate anterior vaginal swellings. As a rule, it is gradual in development; it is occasionally associated with strangulation. It is not painful, and incapacitation for work comes from the inconvenience of the mass. Disturbances of the bladder and bowels occur occasionally, more frequently with the anterior type.

During labor vaginal hernia may appear suddenly, with alarming symptoms of shock and evidence of intestinal obstruction due to incarceration from impingement and dragging of the hernial pouch between the fetal head and the pelvic outlet. In such cases, however, an asymptomatic outpouching prior to labor may be presumed. This condition is treated by pushing the head above the pelvis and reducing the hernia. In Hundley's third case a hernia which appeared in the seventh month was maintained in reduction by tampon until full term delivery.

COMPLICATIONS

In addition to errors arising from mistaken or incomplete diagnosis, various complications, with varying import, may occur in cases of vaginal hernia. The most common is the combination of vaginal hernia with cystocele, rectocele or uterine prolapse, at times resulting in neglect of one or the other condition. Bueermann, in his series of 76 cases, noted complications in 20, as follows:

	No. of Cases
(a) Interference with normal delivery	10
(b) Hernia incised or excised because of error in diagnosis with death	3
(c) Pelvic abscess following delivery with spontaneous recovery	2
(d) Rupture of hernia with evisceration and death	2
(e) Rupture of hernia with recovery	1
(f) Rupture of hernia during delivery with recovery	1
(g) Death from incarceration of vaginal hernia	1

Tumors, conditions of the heart and kidney which produce ascites, obesity and other abnormalities should be considered in terms of complications, not only as factors creating increased intra-abdominal pressure and thus causing enterocele, but also as conditions endangering the efficacy and permanency of operative procedures.

PROGNOSIS

Vaginal hernia may cause considerable discomfort, often preventing work, but does not endanger life unless strangulation occurs, when immediate surgical intervention becomes imperative. Reduction is usually possible, while surgical repair offers excellent promise of permanent cure.

TREATMENT

Treatment is preeminently surgical. Operation is performed by either an abdominal or a perineal approach. The latter, usually following the procedure of Kelly, is particularly useful in cases of old or debilitated patients or those in which vaginal hernia is accompanied by rectocele or cystocele, and gives an excellent view of the hernia and its ring. The vaginal mucosa is longitudinally incised over the mass and the sac carefully exposed by blunt dissection. If any intestinal loop is in the sac, the patient's hips are elevated to effect reduction. The sac should then be opened with the greatest of care and cut short and the stump sutured behind the cervix, or the sac may be sutured whole to the uterine surface as additional support to the pelvic floor. The pelvic floor is then closed by cross or purse string sutures, a process

in which living sutures may occasionally be required, after which perineovaginal defects are corrected, excess vaginal tissue trimmed off and the operative wound routinely closed. When the sac is too adherent to be dissected free, the cavity should be obliterated by scarification, the peritoneal surface sutured as high as possible and the pelvic floor then firmly closed over the opening.

In the presence of a good perineum, when the patient is otherwise healthy, the abdominal route as used by Moschowitz is more usually chosen, as it permits easier reduction of the hernia with resection of the intestine if indicated and the sac can more easily be identified and the hernial opening more firmly closed. In this the hernia is reduced and the sac then invaginated, folded on itself and sutured to the pelvic floor as reinforcement, or the sac may be closed by a series of superimposed purse string sutures starting at its base and finally ending with suture of the pelvic floor and the uterosacral ligaments but without inclusion of the uterus. At times it may be necessary to use a combined abdominoperineal approach to deal with the vaginal hernia and its complications. In any case, it is advisable to implant ureteral catheters before operation. The danger of inclusion of the ureters in repair of the pelvic floor is considerable.

Reduction of weight is important, preoperatively and postoperatively, in lessening the operative mortality, but particularly in removing the concomitant intra-abdominal pressure, which tends to break down the repaired pelvic floor and cause recurrence of the hernia. Likewise other factors causing increased intra-abdominal pressure should be removed by appropriate medical and surgical procedures.

SUMMARY

Today there are complete disorganization in the literature and a lack of reliable statistical data on vaginal and pelvic hernias because of multiplicity and uncertainty in terminology and diagnostic requirements and because of inadequate examinations and reports and mistaken interpretations to be noted in many writings.

As interpreted by certain writers, vaginal hernia is a rare condition, a subvariety of pelvic hernia, appearing in the anterior or posterior fornix.

There have been 26 reported cases of vaginal hernia to date by the strict analyses of Miles or 83 by the broader interpretation of Bueermann, who accepted the diagnosis of the examining physician.

A case report of vaginal hernia is presented, with the first reported microscopic pathologic examination of involved tissues, indicating a pathologic basis for the formation of hernia. This is an aneurysmal relaxation of degenerative scar tissue resulting from obliterative endar-

teritis and may be expected in senile and arteriosclerotic patients, in the absence of traumatic and congenital changes and as contributing factors with them.

Congenital maldevelopment, defects and variations in the pelvic floor are main predisposing factors to vaginal hernia, and trauma at birth, a chief contributing factor.

Vaginal hernia frequently is not diagnosed on the first examination or operation and must be differentiated from various pelvic and vaginal conditions, particularly rectocele, cystocele and prolapsus uteri.

Vaginal hernia as a rule causes only discomfort. In about 1 out of 4 cases the condition is complicated, and in 30 per cent of these it terminates fatally. If the condition develops during labor, the signs may be those of shock and intestinal obstruction; the treatment in this case is immediate return of the head and reduction of the hernia. Obstruction and strangulation from other causes demand immediate surgical intervention.

The treatment is surgical, by an abdominal, a perineal or a combined approach, following an appropriate recognized technic. The insertion of ureteral catheters prior to operation is advised.

All factors, including obesity and tumors, which cause increased intra-abdominal pressure should be corrected by appropriate surgical and medical procedures, as important preoperative, operative and post-operative prophylactic measures.

BIBLIOGRAPHY

- Barker, F.: Vaginal Hernia or Vaginal Enterocoele, *Am. J. Obst.* **9**:177, 1876.
- Birchenall, J.: Vaginal Hernia: Perforation of Ileum Under Sudden Violence, *Brit. M. J.* **2**:182, 1869.
- Black, W. T.: Posterior Vaginal Hernia: Report of Case, *Am. J. Obst. & Gynec.* **27**:837, 1934.
- Breisky, A.: Die Krankheiten der Vagina, in Billroth, T., and Lücke, A.: *Deutsche Chirurgie*, Stuttgart, Ferdinand Enke, 1886, vol. 60.
- Bueermann, W. H.: Vaginal Enterocoele, *J. A. M. A.* **99**:1138 (Oct. 1) 1932.
- Caillot, J.; Rochet, E., and Contamin, R.: Case of Perforation After Curettage of the Posterior Cul-de-Sac with Protrusion of the Sigmoid Treated by Total Abdominal Hysterectomy, *Bull. Soc. d'obst. et de gynec.* **24**:478, 1935.
- Cervenansky, J.: Perineal Hernia, *Bratisl. lekár. listy* **16**:89, 1936.
- Chase, H. C.: Levator Hernia (Pudendal Hernia), *Surg., Gynec. & Obst.* **35**:717, 1922.
- Crossen, H. S., and Crossen, R. J.: *Operative Gynecology*, ed. 4, St. Louis, C. V. Mosby Company, 1930, p. 241.
- Derby, D. E.: Pelvic Muscles and Fasciae, *J. Anat. & Physiol.* **42**:107, 1907-1908.
- Dew, J. H.: Posterior Vaginal Hernia, *J. M. A. Georgia* **23**:349, 1934.
- Erdman, S.: Hernia, in Nelson Loose-Leaf Living Surgery, New York, Thomas Nelson & Sons, 1927, vol. 4, p. 663.

- Etheridge, J. H.: Case of Anterior Vaginal Enterocoele, *J. A. M. A.* **8**:162 (Feb. 5) 1887.
- Green, E. K., and Buzzell, L. K.: Vaginal Hernia, *Minnesota Med.* **14**:162, 1931.
- Hartmann, H.: La hernie vaginale et son traitement, *Ann. de gynec. et d'obst.* **12**:351, 1916.
- Hugnier, M. A.: Un cas de hernie vaginale (elythrocele), *Paris chir.* **9**:496, 1912.
- Hundley, J. M.: Treatment of Vaginal Hernia Associated with Prolapsed Uteri, *South. M. J.* **20**:345, 1927.
- Lathrop, H. A.: Operation for the Cure of Vaginal Hernia, *Boston M. & S. J.* **168**:578, 1913.
- Masson, J. C.: Prolapse, Cystocoele, Rectocoele and True Vaginal Hernia, *J. A. M. A.* **99**:1143 (Oct. 1) 1932.
- and Semon, H. E.: Vaginal Hernia, *Surg., Gynec. & Obst.* **47**:36, 1928.
- Michelson and Lukin, cited by Erdman.
- Miles, L. M.: Pelvic Hernia; Posterior Vaginal Hernia, *Surg., Gynec. & Obst.* **42**:482, 1926.
- de Modena, V.: Vaginal Hernia of Lateral Cul-de-Sac, *Ann. paulist. de med. e cir.* **32**:541, 1936.
- Moschowitz, A. V.: Perineal Hernia, *Surg., Gynec. & Obst.* **26**:514, 1918.
- Prolapse of the Rectum, *ibid.* **15**:7, 1912.
- Smellie, cited by Hundley.
- Stearns, R. J.: Vaginal Hernia of Douglas' Culdesac, *Am. J. Obst. & Gynec.* **31**:144, 1936.
- Sweetser, H. B.: Vaginal Hernia, *Ann. Surg.* **69**:609, 1919.
- Symington, J.: Contribution to the Normal Anatomy of the Female Pelvic Floor, *Edinburgh M. J.* **34**:788, 1888-1889.
- Taylor, J.: Case of Vaginal Hernia, *Lancet* **1**:205, 1831.
- Thomas, T. G.: Vulvar and Vaginal Enterocoele, *New York M. J.* **42**:705, 1885.
- Williamson, W. L.: Enterocoele: Case Reports, *Memphis M. J.* **9**:1272, 1932.
- Zeigenspeck, cited by Bueermann.
- Zuckerkandel, O.: Beiträge zur Lehre von den Bruchern im Bereiche des Douglasschen Raumes, *Deutsche Ztschr. f. Chir.* **31**:590, 1891.

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REVIEW OF UROLOGIC SURGERY

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KIDNEY

Tumor.—Smith¹ stated that either the lumbar or the transperitoneal approach may be used for removal of a tumor of the kidney. In a series of 50 cases of renal and ureteral neoplasms, the kidney was removed transperitoneally in 22 and by the lumbar route in 22. Indications for the selection of the lumbar route are: (1) uncertain diagnosis; (2) small size of the mass; and (3) probability that the growth is pelvic rather than cortical. The transperitoneal route is chosen for removal of large cortical tumors. It allows examination of the abdomen for metastatic growths before the tumor is disturbed.

When the intestines are walled off from the upper part of the abdomen on the affected side, the tumor will be seen beneath the posterior portion of the peritoneum. It may be exposed through an incision made in the overlying peritoneum or in the parietal peritoneum 1 inch (2.5 cm.) outside the ascending or descending portion of the

1. Smith, G. G.: Surgery of Renal Tumors, J. Urol. **39**:308-313 (March) 1938.

colon. The colon, with the posterior peritoneum, is then rolled inward, the entire renal fossa being exposed.

A tumor of the renal pelvis rarely reaches a size which requires the use of the transperitoneal approach. For a tumor in this location removal of the entire ureter together with that portion of the vesical wall through which the ureter passes is an essential part of the operation. In 6 of Smith's 7 cases of ureteral tumor, there was a growth either in the intramural portion of the ureter or arising from the ureteral meatus.

Accidental tear of the vena cava is encountered usually in an operation on the right kidney and occurs in one of three ways: (1) inclusion of a portion of the vessel in the mesial clamp on the renal vessels, (2) tearing of a portion of the vena cava which is adherent to the kidney as the latter is mobilized and (3) avulsion of the renal vein at its site of entrance into the vena cava by undue traction on the renal pedicle. Five methods have been advocated to control the bleeding: (1) packing, (2) partial or lateral ligation, (3) complete ligation, (4) application of clamps, which are left in place, and (5) suture of the tear. Packing is the least satisfactory; lateral ligation is also untrustworthy. Apparently, complete ligation may be done. Pfaff reviewed 19 cases in which complete ligation was performed, with 6 deaths. The ligation must be below the entrance of the left renal veins; otherwise death from uremia will follow. Walters and Priestley stated the opinion that accurate application of large, smooth-jawed, curved clamps to the defect in the vena cava is a satisfactory method of closure. The clamps should be left in place for one week; then they should be gently loosened and removed in twelve to thirty-six hours. Suturing with oiled silk is the ideal method of closure.

The results of nephrectomy for renal tumor are difficult to estimate. Recurrence of such a tumor fifteen years after operation has been reported by Muir and Goldsmith, and a number of like cases, in which the tumor recurred nine, ten and twelve years after nephrectomy, have been reported by other writers.

With reference to the surgical approach to a tumor of the kidney, Cabot² expressed entire accord with the view that the lateral approach is desirable for a tumor of the renal pelvis. In dealing with a tumor of the renal parenchyma, the operator from the outset should have complete control of the blood supply and should be concerned not exclusively with the tumor but also with the whole surrounding region. The exposure of such a tumor cannot be complete through the lateral approach. An anterior approach should allow exposure of the entire region and should be begun not in the loin but at the outer border of the rectus

2. Cabot, H., in discussion on Symposium on Renal Tumors, *J. Urol.* 39:314-315 (March) 1938.

muscle, where the peritoneum should be opened for exploration. If the tumor is inoperable, the wound can be closed promptly and without damage to the patient.

Cabot² called attention to the use of the parietal peritoneum for walling off the intestine. This enables the operator to avoid the use of gauze packing or other noxious substances, which seem readily to produce shock. The peritoneum is an excellent agent for walling off the intestine completely. Cabot pointed out that it is essential to proceed cautiously in approaching the pedicle and to tie all the afferent veins carefully, because the tearing of the veins over the fatty capsule often will be troublesome, and the resulting loss of blood is the essential contributing factor in the mortality. Division of the ureter should be made early; then the pedicle is cared for. When the pedicle has been secured, the problem is solved.

Bell³ offered a classification of renal tumors, with observations on the frequency of occurrence of the various types. His paper was based on the study of records of approximately 30,000 necropsies.

The following classification corresponds with that used by the majority of writers:

- I. Renal tumors occurring in children
 - A. Wilms' tumor, 5 cases
 - B. Multiple tumors with tuberous sclerosis, 1 case
- II. Renal tumors occurring in adults
 - A. Parenchymal
 - 1. Fibroma
 - 2. Leiomyoma
 - 3. Lipoma and liposarcoma
 - 4. Fibrosarcoma, 1 case
 - 5. Hemangioma, 1 case
 - 6. Wilms' tumor
 - 7. Adenoma
 - 8. Adenocarcinoma

} 149 cases

- B. Pelvic
 - 1. Papilloma, 1 case
 - 2. Carcinoma, 3 cases

Bell found only 5 renal tumors in children in the series of 30,000 postmortem examinations, in which children were proportionately represented. Except for the multiple tumors of tuberous sclerosis, all the tumors were of the Wilms type. Examples of hypernephroma (adenocarcinoma) were not found among children. Wilms' tumor occurs in the first decade of life and is highly malignant, only an occasional cure being reported. The tumor is large and fleshy; it does not have the

3. Bell, E. T.: A Classification of Renal Tumors with Observations on the Frequency of the Various Types, *J. Urol.* **39**:238-243 (March) 1938.

yellowish or whitish color characteristic of tumors occurring in adults. Histologically two varieties are distinguished, adenosarcoma and rhabdomyosarcoma. Bell found 3 cases of the former and 2 of the latter.

Renal Tumors in Adults.—The vast majority of renal neoplasms develop in the parenchyma, which includes all of the renal substance except the pelvis and the connective tissue surrounding it. Fibroma of the cortex is a subcapsular growth rarely more than a few millimeters in diameter. Leiomyoma is a tumor of fairly frequent occurrence. It is seldom more than 5 mm. in diameter, and is situated immediately beneath the capsule in most instances. It probably originates from capsular, smooth muscle or from the muscle of blood vessels. Lipoma is comparatively rare and usually is very small. It occupies the outer portion of the cortex, under the capsule. Several large benign lipomas and a few liposarcomas have been reported. Fibrosarcoma of the kidney is rare. Most of the tumors which appear to be sarcoma on casual microscopic examination prove to be undifferentiated carcinoma on examination of a number of sections from different parts of the tumor. Hemangioma is a rare tumor which does not produce symptoms unless it erodes the renal pelvis, in which case hematuria ensues. In rare instances Wilms' tumor occurs in an adult. The structure is usually that of adenosarcoma. No instance of occurrence of this tumor in an adult was found. Adenoma and adenocarcinoma were discussed together because the distinction between them is somewhat arbitrary.

A survey of 383 cases of Wilms' tumor, collected from the literature or observed personally by McNeill and Chilko,⁴ revealed a poor prognosis and a mortality rate of more than 90 per cent.

Six types of treatment have been followed: (1) nephrectomy alone, which in the opinion of the majority of surgeons offers the only chance for the patient's recovery; (2) serum therapy in conjunction with nephrectomy (Coley reported a good result from this method); (3) roentgen therapy to reduce the size of the tumor and to kill the embryonal cells, followed by nephrectomy (fewer than six urologists have followed this procedure); (4) roentgen therapy followed by nephrectomy and subsequently by another course of roentgen treatment (only a few surgeons have followed this procedure); (5) nephrectomy followed by roentgen treatment to destroy any residual malignant embryonal cells, and (6) roentgen therapy alone (only 2 successful results from this procedure have been reported, and in each of these instances treatment was given over a period of three to three and a half years). One of the patients (of Pohle and Ritchie) was alive and in

4. McNeill, W. H., Jr., and Chilko, A. J.: Status of Surgical and Irradiation Treatment of Wilms' Tumor and Report of Two Cases, *J. Urol.* **39**:287-302 (March) 1938.

excellent health at the time of the report, three years and eight months after this type of therapy was begun; in the other case the patient was alive and well three years after institution of radiation therapy.

Kutzmann⁵ stated that squamous cell carcinoma of the renal pelvis is of infrequent occurrence. A review of the literature indicated that ability to recognize it clinically has increased in recent years. In all, 81 authentic cases have been reported. Renal tumors comprise 0.25 to 0.5 per cent of all tumors; of these, 6.4 per cent occur in the renal pelvis. Squamous cell carcinoma forms about 17 per cent of the latter group, making 1 in 18,518, or a general incidence of approximately 0.005 per cent.

There is no pathognomonic clinical syndrome. Hence, the diagnosis has never been made preoperatively. The disease has an insidious onset and runs a rapid and fatal course. The only known treatment is nephrectomy. The prognosis is poor, there being no five year cures on record.

Squamous cell carcinoma of the renal pelvis is associated with chronic renal infection and with calculus in more than half the cases.

Squamous cell carcinoma of the renal pelvis presents a paradox, because it is an epithelial growth derived from tissues of mesothelial and entodermal origin. This occurrence can be explained if one assumes the presence of a protective metaplastic process, that is, leukoplakia, on the renal pelvic mucosa, which with continued irritation undergoes malignant degeneration. Leukoplakia, therefore, is to be considered the precursor of squamous cell carcinoma.

Kutzmann reported 1 case of squamous cell carcinoma. The malignant growth was associated with (1) leukoplakia; (2) intense, chronic and destructive pyonephrosis with superimposed infection; (3) calculus, and (4) metastatic involvement of the lymph nodes of the renal pedicle.

Suppuration.—Philippart⁶ stated that he would prefer to abandon the old method of classification of suppuration as hematogenous or ascending, as these terms are derived from mental concepts and do not represent clinical entities. He would return definitely to the use of the anatomicopathologic terminology and speak of pyogenous nephritis, which may appear in any one of three forms: (1) miliary pyogenous nephritis, (2) anthracoid pyogenous nephritis (resembling giant anthrax) and (3) confluent pyogenous nephritis (single or multiple abscess), which includes pyonephrosis.

The diagnosis, which is difficult with the extremely acute form and with the latent form of the disease, is generally easily made in the

5. Kutzmann, A. A.: Squamous Cell Carcinoma of the Renal Pelvis, with Special Consideration as to Etiology, *J. Urol.* **39**:487-505 (April) 1938.

6. Philippart, R.: Suppuration of the Renal Parenchyma, *Kong. d. internat. Gesellsch. f. Urol.* **2**:228-238, 1937.

average case. The diagnosis is based on the classic somatic symptoms: the discrete bacteriuria, the presence of leukocytosis and the results of roentgen examination. Ascending pyelographic and intravenous urographic examinations usually will reveal the most important information.

In considering treatment one must take into consideration the possibility of involvement of the opposite kidney, the possibility of spontaneous cure and the infrequent need for surgical intervention as an emergency measure in such cases. Except for the hyperacute forms of the disease, medical treatment should be tried first, together with physical therapeutic, dietetic and biologic measures. Such treatment may delay the need for surgical intervention, if it does not make it unnecessary. Such intervention, when it becomes inevitable, should be essentially conservative and should be performed in such a way as to minimize trauma. Careful postoperative measures should complete the treatment. These should consist of the following procedures: (1) simple incision of the walls in cases of perinephritic abscess, (2) decapsulation and electrocoagulation in cases of miliary pyogenous nephritis, (3) enucleation [with the electric knife] of the necrotic mass in cases of pyogenous anthracoid nephritis and (4) opening of the intrarenal abscess or of the pyonephrotic lesion in cases of confluent pyogenous nephritis.

In the majority of cases correct drainage and suitable irrigation will bring about complete cure.

If nephrectomy becomes necessary, it should be done in two stages, except in cases in which it can be performed with exceptional facility. A short interval between the two stages allows the condition of the infected organ to improve and the opposite kidney to regain better function.

Lasio⁷ stated that in the study of nonspecific renal suppuration one must bear in mind two fundamental principles: (1) the precise distinction between various grades of suppuration and (2) the concept of the urinary system as a whole, rather than as made up of separate segments. Only with these criteria in mind is it possible to follow the development of suppuration in all its stages, which are, in order, as follows: pyelitis, pyelonephritis (circumscribed), diffuse pyelonephritis (miliary), solitary abscess of the kidney, pyonephrosis, and contracted kidney (post-pyelonephritis).

On the basis of a study of 418 cases of renal suppuration encountered in the urologic clinic of the University of Milan in a period of ten years (1923 to 1932 inclusive), Lasio reached the following conclusions:

The process of endorenal suppuration and all its varieties may be reduced to a single anatomicopathologic process consisting of two fundamental factors, namely suppuration and fibrosis, which are associated

7. Lasio, G. B.: Suppurations of the Renal Parenchyma. *Kong. d. internat. Gesellsch. f. Urol.* 2:212-225. 1937.

in various proportions to constitute a unitary process, the stages of which pass from the initial punctiform abscess to the terminal phase of complete destruction of the organ. These are not different forms; they are only different stages, for the most part clearly distinguishable, and are associated with renal suppuration in every case.

In the grave, diffuse forms of suppuration, the hematogenous route is the most frequent, whereas with subchronic suppuration of slow course and less stormy development the lymphogenous route holds first place. The latter route well explains the passage of micro-organisms from primary sites in the adnexal, perivesical and ureteral regions to the urinary system above. In reality, the pathogenesis of renal infections cannot be explained on the basis of any single route of penetration. Assumption that more than one route of penetration has contributed to the final result is always necessary to a correct interpretation of such phenomena.

With reference to methods of diagnosis, Lasio paid most attention to the presence of pyuria, to search for its origin and to examination of renal function. Typical of the miliary form is local pain, spontaneous or induced, and unilateral hypoazoturia. The urographic findings are characteristic in the different forms of the disease. In cases of simple pyelitis and pyelonephritis these findings are negative; in cases of pyonephrosis and solitary abscess, urographic examination gives invaluable information; in cases of the miliary form of the disease, urographic examination is of value for the negativity of its results.

In treatment, permanent drainage of the urinary system holds first place; this may be total (permanent drainage by a catheter left in the bladder) or partial (permanent drainage by a catheter left in the renal pelvis). Lasio proceeded at once to consider nephrectomy in cases of extensive or limited pyonephrosis and in cases of diffuse miliary nephropylitis. In a considerable number of cases of the latter, however, he has carried out conservative treatment, associating nephrolysis with permanent pyelostomy, and obtained results that were truly satisfying. Such therapy, however, calls for early diagnosis and for good resistance on the part of the patient.

Dos Santos⁸ said that whereas the essential problem of renal suppuration is certainly that of therapy, there is a point in the classification of such an infection that should be clarified. The important thing is not to distinguish between descending and ascending infections but to distinguish between hematogenous infections of the parenchyma and infections of the excretory apparatus, which are nearly always ascending

8. Dos Santos, R.: Suppurations of the Renal Parenchyma, Kong. d. internat. Gesellsch. f. Urol., 1937, vol. 2.

but sometimes descending in type. He was concerned in this report only with hematogenous infections, which constitute a true nosologic entity.

His comments do not reflect the skepticism of some authors with regard to intravenous chemotherapy. In cases of staphylococcic and streptococcic infections, especially good results have been obtained by administration of mercurochrome, so that in some cases a contemplated operation has become unnecessary. For good results large doses are necessary, and these must be given early in the course of the disease. The results will be more certain if instead of the intravenous route the arterial route by way of aortic puncture is chosen. This is because urinary antiseptics administered orally or even intravenously are too dilute when they reach the kidney to be maximally effective. The efficacy of the urinary antiseptic is dependent on the concentration of the drug as it passes through the epithelial tubules of the kidney. Therefore, intra-arterial administration is favored. Dos Santos emphasized the fact that the aorta is the most direct and the most rational route for administration of drugs in the treatment of hematogenous infections of the kidney. The technic of performing such an injection is simple. The injection is absolutely harmless, and there is practically no pain associated with it, according to the author.

Early treatment is necessary if good results are to be obtained. If treatment is instituted within the first two weeks of onset (in cases of moderate gravity) there is every chance that arterial injections will overcome the infection. If one waits longer, the foci of infection may be too extensive, with formation of confluent abscesses or perirenal suppuration which render surgical intervention mandatory.

Of the author's last 40 patients who had hematogenous suppuration, 12 were seen and treated in the first or second week of the disease. All of these were cured without operation, intra-aortic or intravenous mercurochrome therapy, associated with renal diathermy, being the only measure used.

Of 28 patients seen after the second week of the disease, 2 were cured without operation and in 1 other a large abscess emptied spontaneously by way of the renal pelvis; the rest of the patients required operation, nearly all having perinephritic foci. In some cases it was necessary still to use mercurochrome to combat the renal foci that continued to develop. In at least 2 cases this prevented the necessity of nephrectomy or, at least, of reintervention.

It should be remembered that injection of an antiseptic directly into the abdominal aorta is the surest way of reaching not only multiple foci in the kidneys but other sites of infection (hepatic and splenic) along the same route.

Lepoutre⁹ stated that he had had occasion to observe 12 cases of abscess of the renal cortex and to operate in 10 of them. It is important to determine (1) the condition of the patient at the time of examination, and (2) the operation to be employed.

Abscess of the renal cortex may present any one of three pathologic pictures: 1. Septicemia of undetermined localization, persisting for several months and followed at length by lumbar pain. 2. Lumbar pain and tumefaction in the region of the kidney, occurring after a short febrile period. In this condition the urine is clear. If the physician is consulted early enough, an abscess of the cortex is discovered promptly. If intervention is late, perinephritic phlegmon has probably developed. 3. Persistent fever after an operation for perinephritic phlegmon. The fever does not diminish, or, if it does, it reappears after considerable time has elapsed. Operation reveals an abscess that is an indication for nephrectomy.

What operation should be performed? In most cases the good sense of the surgeon will indicate the type of intervention required. A kidney that has been transformed into a purulent sponge justifies the performance of nephrectomy; localized abscesses should be incised and dressed after decapsulation. A difference of opinion regarding treatment of a true carbuncle exists. In the 2 cases observed by Lepoutre, nephrectomy was carried out.

In certain cases of grave pyelonephritis in which nephrectomy might have been regarded as justifiable, Lepoutre drained the renal pelvis, performed decapsulation and brought about a cure. A condition of this kind is not simple abscess of the cortex. This conservative treatment of severe pyelonephritis merits attention.

Fey¹⁰ stated that in dealing with suppuration of the renal parenchyma it is important to distinguish between secondary complications of some renal infection, which will clear up after the primary infection (of which the colon bacillus is the causative agent) has been overcome, and infections due to the staphylococcus. The first may be common radiating nephritis; not only, however, may it become pyelonephritis or pyonephrosis, but it may assume that clinical picture to which Motz has given the name "pyonephritis." One must then suspect an abscess of the parenchyma and intervene by performing nephrostomy or nephrectomy. Infections caused by the staphylococcus, on the contrary, strike quickly, attacking the renal parenchyma but not involving the excretory tract unless one of the collections of pus within the paren-

9. Lepoutre, C.: Suppurations of the Renal Parenchyma, Kong. d. internat. Gesellsch. f. Urol., 1937, vol. 2.

10. Fey, B.: Suppurations of the Renal Parenchyma, Kong. d. internat. Gesellsch. f. Urol. 2:179-182, 1937.

chyma should open, not as usual into the surrounding perirenal tissue, but into the excretory passages by way of a calix. In such a case the clinical picture is different: it is that of septicemia, a generalized process, associated with production of clear urine; it may not even be recognized as being situated in the renal parenchyma unless a systematic search is made for the origin of the intense pain in the costomuscular angle, on which diagnosis is based.

In treatment, the main thing is to know when to intervene. This is particularly difficult to determine in the presence of subacute infection. There are two arguments against early operation. The first is that the condition may improve spontaneously or without intervention. This argument has a certain value, but it should be remembered that spontaneous resorption of an abscess occurs slowly, requiring months rather than weeks. The process often is interrupted by relapses, which may leave a sclerotic kidney with diminished function, so that cure occurs more slowly and less satisfactorily than it would have done if operation had been carried out. The second argument against early intervention is that if one waits one may localize lesions that were at first diffuse and thus may be able to perform a conservative operation, whereas if early operation is done the diffuse appearance of the lesions may lead one to conclude that nephrectomy is necessary and to remove a kidney that might have been saved.

The second argument has special force in cases of miliary abscess, because this condition is sometimes bilateral and may be simultaneously medullar and cortical. Decortication is often insufficient, and one may easily be led to do a nephrectomy. It seems logical, therefore, not to intervene prematurely.

The situation is different in the presence of localized forms of the disease (single abscess or few abscesses; anthrax of the kidney). In such cases temporization has no place and is likely to lead to a reaction of perinephritis which will make eventual operation all the more difficult.

In the first eight days the kidney is free and is easily exteriorized; its surface can be examined throughout to determine whether all the abscesses are draining properly. Later, operation becomes difficult and dangerous; perinephritis develops and fixes the kidney, so that not only is its exteriorization made impossible but renal exploration becomes difficult and dangerous.

Fey therefore advised late intervention in cases of miliary disease and operation as early as possible if focal lesions are present. Pyelographic study is an important aid in reaching a decision. The presence of deformations in the pyelogram is an argument for immediate intervention.

Marinescu¹¹ stated that suppuration of the renal parenchyma, that is to say, pyonephritis, originates by way of the blood stream and is usually caused by the colon bacillus or by the staphylococcus. Sometimes the streptococcus and other microbes may be associated organisms.

The colon bacillus more frequently causes miliary abscesses in the cortex of the kidney, whereas the staphylococcus produces anthracoid furuncle of the kidney by means of emboli which lead to more or less extensive renal necrosis. In most cases perinephritic abscess follows, owing to the opening of the renal abscess into the perirenal zone.

The symptoms of suppuration of the kidney are those of extensive pyemic infection, and the syndrome is completed by clinical signs referred to the lumbar region and by urinary symptoms. Signs of perinephritic abscess often hold first place, and it is only by careful scrutiny of the kidney during operation that one may perceive the suppuration within the organ. Modern methods of examination, especially urographic study, may confirm the clinical diagnosis. The prognosis is grave if operation is not performed. Even after the most cautious operations the mortality remains high.

For abscess of the cortex, decapsulation of the kidney is often sufficient. More often, however, nephrostomy should also be carried out. Cauterization with the galvanocautery is indicated for small abscesses. For a small furuncle of the kidney, cauterization and curettage should be carried out; drainage by means of antiseptic gauze may lead to cure. Prompt nephrectomy is indicated if there is extensive destruction of the kidney. When a perinephritic phlegmon is present, the collection of pus must be opened and the kidney carefully controlled for several days afterward if fever persists. A fistula frequently becomes established, and the cicatrized and sclerotic kidney loses its function; when this occurs the kidney must be removed secondarily, a procedure accomplished only with great difficulty.

Beer¹² stated that the subject under discussion should be limited to primary parenchymal infections whether caused by cocci or by bacilli. The coccic infections are the more interesting, and although many are readily diagnosed there is a large group that may present serious difficulties.

Roentgenologic examination should be done in all cases. Both the simple roentgenogram and the urogram may facilitate diagnosis. In Beer's last series of 43 cases in a total of 104 cases of cortical abscess caused by cocci (usually *Staphylococcus aureus*, rarely *Staphylococcus*

11. Marinescu, G.: Suppurations of the Renal Parenchyma, Kong. d. internat. Gesellsch. f. Urol., 1937, vol. 2.

12. Beer, E., in discussion on Symposium on Suppuration of the Renal Parenchyma, Kong. d. internat. Gesellsch. f. Urol. 2:238-240, 1937.

albus or *Streptococcus*), roentgen examination helped in confirming the diagnosis in more than 50 per cent.

Tuberculosis.—The time-honored conception that renal tuberculosis is primarily unilateral, that it is a surgical condition and that nephrectomy is indicated when the diagnosis has been made has been undermined by conclusions drawn by some observers from recent experimental and pathologic studies. It is contended that the disease is bilateral from the onset, that this early bilateral tuberculosis may heal spontaneously on one or both sides and that a chance of cure by medical means should be given. Nephrectomy should be postponed, at least until the lesion is far enough advanced to allow for establishment of some immunity.

Hinman¹³ attempted to reconcile the discrepancies in these opposing conceptions by a study of 300 patients with renal tuberculosis, on 181 of whom nephrectomy had been performed, and by a discussion of certain practical points regarding diagnosis and treatment.

He distinguished preclinical from clinical tuberculosis and said that findings in cases of the preclinical form should not influence the management of the clinical type. Associated with active extra-renal tuberculosis, bacilluria without pus may be present, and on microscopic examination of the kidneys minute bilateral lesions may be found. The bacilluria may disappear, and the inference that the early lesions have healed spontaneously or under medical treatment is clear. The lesion in clinical tuberculosis, on the other hand, is usually unilateral and will not heal spontaneously. Nephrectomy is indicated. The diagnosis is made by the finding of tubercle bacilli and pus in the urine on several examinations.

When pus and tubercle bacilli are found in the urine from each kidney at the time of cystoscopic examination, pyelographic study is not needed, and its use should be condemned. The diagnosis should not depend on excretory urograms, but these may be the means of obtaining valuable information about the condition of the opposite, nontuberculous kidney and if unsatisfactory may be supplemented by retrograde pyelographic examination, all known precautions being taken against contamination of the nontuberculous kidney.

A sterile pyuria without the presence of tubercle bacilli may be confusing but can be distinguished by its response to treatment. The terminal stages of some pyogenic infections clear up with irrigations of the bladder and the renal pelvis. Amicrobic pyuria, which is frequently reported in the foreign literature, responds promptly to administration of neoarsphenamine.

13. Hinman, F.: *Tuberculosis of the Kidney*, Surg., Gynec. & Obst. 66:329-347 (Feb. 15) 1938.

The clinical form of renal tuberculosis is unilateral in 85 per cent of cases when first diagnosed, and if the condition is localized in the kidney, nephrectomy is 100 per cent curative. When it has spread to the bladder or genital tract, nephrectomy is still 60 to 70 per cent curative.

Formation of persistent sinuses after nephrectomy is the result of tuberculosis of perineal tissues or of contamination and is not the result of tuberculosis of that portion of the ureter which has not been removed. As much of the ureter as is accessible should be removed, but complete ureterectomy is unnecessary, as the additional operative work required by it may be detrimental.

Alcorn and Buchtel¹⁴ briefly reviewed the literature pertaining to cultural findings and microscopic studies of the urine in cases of renal tuberculosis. They reviewed records of 1,269 cases of coccic and bacillary infection of the urinary tract encountered at the Mayo Clinic. In only 85 cases did the urine contain *Mycobacterium tuberculosis*. The p_H of the urine was noted. The urinary sediment was stained with Gram's stain, and urinary cultures were made. The hydrogen ion concentration of the urine was estimated by colorimetric methods.

The organism most frequently found in this series of cases was *Escherichia coli*. This was the only organism found in the urine in 743 cases. In these cases the p_H of the urine varied from 4.6 to 7.7, and in approximately half it varied from 5.3 to 5.9. In cases in which the infection was attributable to a single type of bacterium, the organism next in frequency was *Aerobacter aerogenes*, which was present in 135 cases. In 61.5 per cent of these, the p_H of the urine ranged from 5.3 to 6.3. In 78 cases in which the infection was attributable to *Myco. tuberculosis*, the p_H of the urine varied from 5.0 to 7.1. In 50 per cent of these it varied from 5.5 to 6.1. With the exception of cases in which urea-splitting organisms were encountered, the p_H of the urine varied slightly in the majority of cases, and it was practically the same whatever organism was found in the urine. These findings certainly weaken the conception that urine from tuberculous kidneys is bactericidal owing to its increased acidity.

In 38 (47.7 per cent) cases of renal tuberculosis, other organisms were associated with *Myco. tuberculosis* in the urine. *Esch. coli* was recovered in 8 cases, whereas in 9 instances the bacteria were identified only by use of the Gram stain. *Streptococcus faecalis* and *Micrococcus* were each present in 4 cases, whereas cocci were identified by staining methods in 20 cases.

14. Alcorn, K. A., and Buchtel, H. A.: The Urine in Renal Tuberculosis: Its Reaction and Associated Bacteria, *J. Urol.* **39**:376-382 (March) 1938.

Alcorn and Buchtel concluded that the finding of ordinary bacteria in the urine does not exclude the presence of renal tuberculosis, because in 44.7 per cent of cases of this disease the urine is infected secondarily. In most cases the urine has a definite acid reaction. In the more frequent pyogenic infections the urine has an equally low acidity. Organisms associated with Myco. tuberculosis in the urine do not appreciably affect the reaction of the urine unless they split urea. Urea-splitting organisms were present in only 7.9 per cent of the cases studied.

Henline and Bray¹⁵ presented histories of 7 patients with urogenital tuberculosis for whom operations on the urogenital tract were performed. All these patients died after postoperative cystoscopic examination. Evidence that any of the deaths (except 1 due to a surgical accident) was either caused or hastened by the urologic procedures was not found.

It was Henline and Bray's impression that the early operative mortality in cases of renal or genital tuberculosis is no greater than that of major operations for other types of infection. The late mortality (between two weeks and five years) is considerably greater, death often resulting from one of the usual terminal stages of tuberculosis, that is, miliary, pulmonary or generalized tuberculosis, tuberculous meningitis or, occasionally, tuberculosis of the remaining kidney.

Although particular gentleness and care always should be exercised in diagnostic or surgical procedures on patients who have tuberculous lesions, Henline and Bray concluded that such procedures rarely, if ever, cause generalized dissemination of tuberculosis or hasten the fatal outcome among patients who eventually die. They concluded that death results from gradual progression of the disease and that the urologic, diagnostic and surgical procedures are merely noncontributory incidents in the course of this progression. Patients seek medical advice because their urologic symptoms are becoming exaggerated, and it is probable that the increasing severity of urogenital symptoms is a manifestation of a progressive tuberculous process in the presence of lowered general resistance.

Early diagnosis and removal of urogenital foci of infection permit the patient to combat more readily the general tuberculous infection under proper medical supervision. Only by such early diagnosis and removal of tuberculous urogenital infection will the morbidity and mortality of patients suffering from such complications be reduced.

15. Henline, R. B., and Bray, J. L.: Urogenital Tuberculosis: Complications Following Diagnostic and Surgical Procedures, *J. Urol.* 39:529-547 (April) 1938.

All patients who have urogenital tuberculosis should be carefully studied to determine the stage of the tuberculous process, and after surgical removal of the focus of infection they should be urged to remain under constant and competent medical supervision.

Dissemination of tuberculosis by urologic procedures has been reported, but it is our opinion that a close analysis of each case will lead to the inevitable conclusion that the cause of the fatal termination was in progress before any urologic manipulation was undertaken.

Certain factors are recognized which when properly utilized may influence favorably the progress of various tuberculous lesions in the urogenital system. Thomas, Kinsella, Stebbins and Petter¹⁶ stated that these methods are not to be used to the exclusion of surgical treatment when operative intervention is indicated and other conditions are favorable for its use. Certain of these, particularly constitutional treatment, the use of heliotherapy and adequate treatment of other tuberculous foci, if properly used may add materially to the chances of recovery, the comfort during convalescence and the prolongation of life of the patient. A broadening of the urologist's horizon, which will permit him to complement or supplement his surgical treatment of genitourinary tuberculosis by some of these other methods, will prove of benefit to his patients and augment his reputation in the handling of patients suffering from this disease.

Ljunggren¹⁷ stated that an ordinary roentgenogram is of value in diagnosis of late renal tuberculosis but is rarely so in determination of the condition in an early stage. A retrograde pyelogram gives more important information than an ordinary roentgenogram, but its use has never become as widespread in Europe as in America. Many urologists of high standing (Casper, Rubritius, Wildbolz and Hinman) oppose it, as they believe it causes extension of the infection.

Excretory urographic study has been of decided advantage in the detection of renal tuberculosis. In Ljunggren's opinion both methods, the retrograde and the intravenous, are now overestimated. More and more cases are reported in which tuberculosis is diagnosed on pyelographic evidence alone and the kidney, in which even the most minute microscopic examination fails to reveal positive signs of tuberculosis, is removed. Ljunggren cited several cases that came under his observation which confirmed this opinion. The condition in these cases turned out to be pyelitis cystica, juvenile malignant renal sclerosis, chronic pyelonephritis or an anomaly. Ljunggren advised against

16. Thomas, G. J.; Kinsella, T. J.; Stebbins, T. L., and Petter, C. K.: Factors Favoring Non-Progression of Certain Tuberculous Lesions of the Urogenital Tract, *J. Urol.* **39**:97-110 (Feb.) 1938.

17. Ljunggren, E.: Zur Röntgendiagnostik der Nierentuberkulose, *Ztschr. f. Urol.* **32**:40-49 (Jan.) 1938.

making the diagnosis of renal tuberculosis on pyelographic evidence alone. He concluded that other diagnostic methods, such as analysis of the urine, cystoscopic study, ureteral catheterization, functional tests and, above all, demonstration of tubercle bacilli (by examination of the smear directly, by culture or by inoculation of guinea pigs) are essential.

Hypertension and Renal Disease.—Boyd and Lewis¹⁸ reported a case of nephrectomy for arterial hypertension which is of considerable surgical interest, because the true condition was brought to light after bilateral simultaneous exposure of the adrenal glands and the kidneys had been performed. This was followed by nephrectomy. The patient was relieved of his symptoms, and his blood pressure returned to normal.

On admission the patient's blood pressure was 200 mm. of mercury systolic and 120 diastolic. Intravenous pyelographic study indicated good secretion of iodide in five minutes from both kidneys. The right kidney had normal delicate calices, a normal extrarenal pelvis and a normal ureter. The adrenal gland was well visualized and appeared normal. The left kidney had very delicate calices. The left renal pelvis was smaller than the right. The ureter was normal.

Exploration of the adrenal gland and the kidney (bilaterally) and nephrectomy (on the right) were performed. The patient was placed on the operating table in Young's position for bilateral simultaneous exposure of the adrenal glands, face downward with the hips flexed at about 55 degrees, the chest and pelvis being elevated on cushions. The abdominal contents sagged between the cushions. The kidneys and the adrenal glands were explored simultaneously. The adrenal glands were normal. The right kidney, which was infarcted, was removed.

The right kidney was 10 by 6.5 by 3.5 cm. and weighed 138 Gm. The appearance of the posterior surface of the kidney was normal except for a bright yellow depressed area 2 cm. wide at the upper pole. This lesion was continuous with a depressed area replacing the cortical substance of the upper half of the anterior surface of the kidney. On section the lesion was found to involve a segment of the kidney from the pedicle, spreading out toward the cortex in the shape of a fan. Infarction was obvious. Thickening of the arterial walls was apparent.

After operation the blood pressure was 120 mm. of mercury systolic and 80 diastolic. Evidence of shock was not present. The patient returned to his home to rest for three weeks and then resumed his normal activities. His blood pressure, reported by his physician, was

18. Boyd, C. H., and Lewis, L. G.: Nephrectomy for Arterial Hypertension: Preliminary Report, *J. Urol.* **39**:627-635 (May) 1938.

130 systolic and 80 diastolic. He felt well and carried on his normal activities.

At operation both adrenal glands were exposed simultaneously, carefully isolated and compared. Some of the nerves were probably severed in the process. Thus, partial denervation of the adrenal glands, as described by Crile, may account for relief of the hypertension, but immediate improvement in the condition did not occur, which is contrary to expectation if this hypothesis were true. It seems probable that the arterial disease of the right kidney was responsible for the hypertension. The infarct was of secondary importance but served to call the operator's attention to the condition. Had the infarct not occurred, nephrectomy probably would not have been done. The clinical result in this case to date seems to justify the use of the procedure.

Leadbetter and Burkland¹⁹ gave a résumé of experimental work on production of hypertension by constriction of the renal arteries of animals, paying particular attention to the fact that partial constriction of only one renal artery results in definite, sustained hypertension.

A case showing the clinical application of the experimental work was presented. The patient was a Negro boy aged 5½ years, with a severe degree of hypertension known to have been present for three years. Apparent cure was effected by removal of an ectopic kidney, the main artery of which was partially occluded.

The cause was found to be an intra-arterial mass of smooth muscle, which was thought to be congenital.

A discussion of theories attempting to explain the mechanism of the production of hypertension in a case of this sort, as well as suggestions for further study of the problem by differential tests of renal function, was offered. The splendid results obtained should stimulate investigation of the kidneys as a possible source of malignant hypertension in cases in which sympathectomy or excision of adrenal glandular tissue is contemplated.

Barker and Walters²⁰ discussed the work of Goldblatt, which has demonstrated that hypertension can be produced experimentally by partial obstruction of the renal arteries. This work has revived the theory which associates hypertension with renal disease. The hypothesis has been advanced by certain investigators that this renal type of hypertension is produced by liberation of some pressor substance within the kidney. This has not yet been definitely proved. Longcope observed

19. Leadbetter, W. F., and Burkland, C. E.: Hypertension in Unilateral Renal Disease, *J. Urol.* **39**:611-626 (May) 1938.

20. Barker, N. W., and Walters, W.: Hypertension Associated with Unilateral Chronic Atrophic Pyelonephritis: Treatment by Nephrectomy, *Proc. Staff Meet., Mayo Clin.* **13**:118-121 (Feb. 23) 1938.

hypertension in 11 of 22 cases of chronic bilateral pyelonephritis. Barker and Walters reported a case of unilateral chronic atrophic pyelonephrosis in which hypertension appeared after chronic pyelonephritis was well developed and in which the blood pressure returned to normal limits after nephrectomy.

The patient was a man aged 42, who came to the Mayo Clinic in November 1937 because of hypertension. Four years previously ureterolithotomy on the right side had been performed, and after this operation he had no further symptoms referable to the urinary tract, although examination at the time of the operation revealed definite hydronephrosis on the right. His blood pressure, which had been determined previously, was normal until August, when it was found to be 200 systolic and 140 diastolic. The right kidney on previous examination had been relatively normal (except for hydronephrosis) until October, when it was found greatly contracted. A familial history of hypertension was not obtained. Examination gave essentially negative results except for generalized evidence of moderate arteriosclerosis. The urine contained erythrocytes (grade 1) and pus (grade 3). All other laboratory studies gave essentially negative results, except that examination of an intravenous urogram showed contraction and distortion of the right kidney. The left kidney appeared normal. Function on the right side was definitely reduced. The blood pressure in millimeters of mercury varied from 232 systolic and 135 diastolic to 170 systolic and 120 diastolic. Nephrectomy on the right side was done; the kidney was found to be approximately half the normal size. It had a very nodular surface. Histologically a considerable portion of the parenchyma was replaced by fibrous tissue. The arcuate and interlobular arteries showed definite thickening of their walls. During the first eleven postoperative days the blood pressure gradually fell to 140 systolic and 100 diastolic. Three weeks after operation the average blood pressure was 135 systolic and 95 diastolic. Two months after operation the patient's blood pressure still remained at 130 systolic and 90 diastolic. At the time of the report it was, of course, impossible to determine what the ultimate result would be in this case.

Hydronephrosis.—Hepler²¹ stated that the intrarenal changes associated with hydronephrosis consist chiefly in anemic atrophy of the parenchyma, induced by back pressure and the effect of pelvic distention and tubular dilatation of the renal circulation. Tubular dilatation is followed by collapse and atrophy, and there is a general degeneration of tissue and relaxation caused by anemia, which in turn favors a more rapid dilatation from back pressure.

21. Hepler, A. B.: Intrarenal Changes in Hydronephrosis, *J. Urol.* 38:593-604 (Dec.) 1937.

The importance of circulatory disturbance to hydronephrotic atrophy was emphasized by experiments in which, in addition to ureteral ligation, the circulation was further disturbed. This resulted in a greatly accelerated rate of development of hydronephrosis despite reduction in urinary output and secretion. Because of the relations of the renal circulation the changes of hydronephrotic atrophy show a group distribution.

After relief of obstruction there is improved circulation with improved function and hypertrophy of the less damaged glomerulotubular units. The repair, like the damage, is not uniform and diffuse but shows group distribution.

Although the changes of hydronephrotic atrophy are constant, the rate of development and the degree of hydronephrosis vary with the situation and the type of obstruction.

Infection may modify profoundly the development of hydronephrosis and the process of repair. In the early stages of obstruction its onset may cause primary atrophy without hydronephrosis. In the later stages of obstruction, after hydronephrosis has progressed, infection may cause secondary atrophy and shrinkage. Likewise, it may hinder the process of repair after relief of obstruction has been accomplished, and infection is an important factor contributing to the failure of operation in such cases.

Walters, Cabot and Priestley²² reported the operative results in 71 cases in which conservative operations had been done for non-calculous hydronephrosis. All cases in which primary nephrectomy was performed, all in which heminephrectomy was done and all in which hydronephrosis was associated with calculi were excluded from the report.

The operative mortality rate in this group of 71 patients operated on at the Mayo Clinic during the past eight years was 2.81 per cent. Secondary nephrectomy was required in approximately 21 per cent of cases. The incidence of secondary nephrectomy during recent years has been materially reduced. Satisfactory follow-up studies were obtained in 46 of the 71 cases. Twenty-five of the 71 were excluded because in 8 cases evaluation of the late results following operation was inadequate, in 15 cases nephrectomy was subsequently performed, and 2 patients died. Various types of operation were performed. These included resection of the renal pelvis with reimplantation of the ureter, division of anomalous vessels supplying the lower pole of the kidney, ureteropyeloneostomy, ureterolysis and miscellaneous proce-

22. Walters, W.; Cabot, H., and Priestley, J. T.: Operative Results in Noncalculus Hydronephrosis: Results in Seventy-One Plastic Operations, *J. Urol.* 38:688-693 (Dec.) 1937.

dures. Nephropexy was performed in 19 cases. In some of the earlier cases nephrostomy was not employed; however, during recent years this has become a routine procedure in association with all plastic operations for hydronephrosis. The importance of using a ureteral "splint" catheter and leaving it in place for a sufficient time after operation was emphasized.

Twenty-six patients were reexamined personally, and urologic investigation was conducted at an appreciable interval after operation. The late results obtained in these cases are classified as follows:

1. Excellent results occurred in 5 cases. The patients were relieved of all symptoms. The renal pelvis, as demonstrated urographically, was definitely smaller than before operation and emptied completely in a normal period.

2. Good results occurred in 8 cases. The patients had complete relief of symptoms, and the renal pelvis was apparently smaller, as shown urographically. The renal pelvis emptied within a reasonable time but not within what may be regarded as normal limits.

3. Improvement occurred in 5 cases. The patients had complete relief of symptoms, and the function of the kidney was as good as or better than before operation, but there was still definite abnormality in the size of the renal pelvis or calices.

4. Improvement failed to occur in 8 cases.

Late results in the remaining 20 cases were evaluated by information obtained from questionnaires. The condition of the patients was recorded as follows: that of 7, good; that of 8, improved; and that of 5, unimproved. The results in all cases, as evidenced by pyelograms and letters, showed the condition of the patients to be as follows: that of 5, excellent; that of 15, good; that of 13, improved; and that of 13, not improved. Therefore, 33 of the 46 patients (71.7 per cent) definitely benefited by the operation.

Pyelitis.—De Beaufond²³ stated that the dominant feature in the pyelitis of pregnancy is atonic dilatation of the excretory apparatus of the kidneys. This dilatation is not uniform throughout the entire tract of the ureter, nor does it exclude contractility, but the contractions differ essentially from the normal extragavidic type, being more widely spaced and deeper, producing massive ejaculations. These manifestations are more pronounced as a rule on the right side; they occur with pregnancy and disappear after parturition. They generally appear at about the fourth month and are more severe at the end of pregnancy. Tonicity and motoricity begin early to show variations, commencing with the ureter, but de Beaufond has found that the most sensitive

23. de Beaufond, F. H.: L'influence de la grossesse sur l'appareil excréteur du rein, Kong. d. internat. Gesellsch. f. Urol. 2:260-267, 1937.

point is the ureteropyelic sphincter, which promptly shows signs of insufficiency. Variations in the urinary circulation also appear: the dilated ureter evacuates its contents slowly, and the delay is often considerable. Its main characteristic is a slowing down, with stasis, followed by evacuation in large quantities.

These manifestations represent a physiologic adaptation in which a mechanical and a dynamic factor are present. The mechanical factor consists not only of the pressure exerted by the gravid uterus but also of the active role played by fetal movements, which strike the ureter and cause contractions and evacuation of urine. This is a subject that has received little study. The dynamic factor reveals itself by the presence of hormones in the blood stream and in the urine. This modified blood nourishes the excretory apparatus, the function of which is to transport the equally modified urine. The usual conditions of function are thus doubly changed. It appears that the dynamic action precedes the mechanical action.

This newly established physiologic equilibrium brings with it functional troubles, of which the pyelitis of pregnancy is the most usual expression. Slowing down of the circulation and stasis within the excretory passages are peculiarly favorable to infection. And yet this pyelitis of pregnancy is by no means as frequent as the new mode of functioning of the urogenital structures would lead one to expect. One is tempted to believe that the hypertrophy of the muscularis and of the mucosa, anatomically observed, represents the development of means of defense, counterbalancing by an increased contractility the atonic dilatation and protecting with a mucous barrier, similarly reenforced, the excretory passages threatened with infection. This view is upheld by the fact that the course of this essential pyelitis of pregnancy is generally benign. In tuberculous conditions this benign course does not prevail. Other pathologic conditions of the excretory passages, however, such as lithiasis, malformations and calculi, are rather well tolerated. Even severe hydronephrosis may fail to give any trouble during pregnancy. In cases in which infection assumes a gravidotoxic form, the origin of this factor lies outside the excretory tract. When complications do arise, the pathologic state of the excretory canal aggravates their results. Early diagnosis is therefore of first importance. Roentgenographic and urographic study, together with catheterization, give invaluable information in the presence of this condition.

Rupture.—The seriousness of rupture of the kidney cannot be determined on the basis of clinical symptoms alone. Domrich²⁴ stated that his experience with excretory urography is still too limited in such cases

24. Domrich, H.: Versuche über die Funktion verletzter Nieren, Ztschr. f. Urol. 32:78-90 (Feb.) 1938.

to give him a complete understanding of the pathologic changes present. It is necessary to know what happens to a kidney in the period after rupture has taken place and how it reacts to slight and severe trauma. Domrich's experiments tend to show what happens during this period. Using rabbits under local anesthesia, he freed the left kidney, traumatized it with his fingers and injected 20 cc. of skiodan immediately after the operation, repeating the injection a few hours later and a few days later.

He obtained the following results. Secretion of the kidney continues after trauma as long as the tissue and the renal blood supply are still intact. During the period of recovery the secretion of the traumatized as well as that of the intact kidney is less than that observed immediately after the trauma. Excretory urographic examination, therefore, can reveal the gravity of the lesion only immediately after the rupture. It indicates which side is involved but does not reveal the extent or type of the lesion.

Hematoma.—Coppridge²⁵ presented a case of spontaneous subcapsular renal hematoma with unruptured capsule. Regardless of the fact that ordinary functional studies before operation showed normal renal function, the microscopic study of the organ revealed definite intercapillary glomerular nephritis. The changes in the vessels of the kidney suggest that the hemorrhage was probably the result of these changes and the associated high renal vascular pressure. These findings support the researches of Hübner and of Polkey and Vynalek in their contention that subcapsular hemorrhages most often are caused by elevation of renal vascular pressure.

Perinephric Cysts.—Henthorne²⁶ reviewed the literature on perinephric cysts and collected 20 cases. The clinical data obtained from this review were discussed.

The average age of the patients was approximately 60 years. The majority were men. In 11 cases there was a history or evidence of obstruction, infection or calculus in the kidney. In 8 cases there were other lesions generally presumed to be congenital anomalies. This fact alone offers some evidence for the congenital origin of peripelvic lymphatic cysts, but the fact that such cysts are usually encountered in patients of advanced age favors the theory that they are acquired.

Perinephric cysts were an incidental finding at necropsy in all cases, with 1 exception, in which the presence of a small cyst was suggested from urographic evidence. The causes of death in these cases were

25. Coppridge, W. M.: Spontaneous Subcapsular Renal Hematoma, *J. Urol.* 39:733-741 (June) 1938.

26. Henthorne, J. C.: Peripelvic Lymphatic Cysts of the Kidney: A Review of the Literature on Perinephric Cysts, *Am. J. Clin. Path.* 8:28-38 (Jan.) 1938.

entirely unrelated to the peripelvic cysts. In 10 cases the cysts were multiple and bilateral; in 3 cases they were multiple and unilateral; and a single cyst occurred in each of 7 cases. The cysts had thin walls and contained a thin, clear albuminous fluid apparently void of any kind of pigment. The cysts varied in size from microscopic lymphatic ectasia to 5 cm. in diameter and had an average diameter of approximately 1 cm. Gross and microscopic pictures were presented. Henthorne concluded that cortical cysts of the kidney are not related etiologically to dilated lymphatic vessels.

Physiology.—Snapper²⁷ stated that in addition to the hydrotropic action of sodium salicylate, sodium hippurate and sodium mandelate, the presence of different colloids in the urine may also contribute to the solution of insoluble salts. In particular, chondroitic sulfuric acid and nucleic acid may help to keep the insoluble salts in solution.

However, for calculogenesis the precipitation of colloids is more important than the precipitation of salts. In the formation and growth of renal stones, flocculation of colloids is the primary process and is followed secondarily by incrustation with salts.

Therefore, it must be possible to prevent the formation of stone by preventing precipitation of colloids. Different organic salts can be used for stabilizing solutions of colloids. Experiments in vitro show that the hippuric acid of the urine must belong to these colloid-stabilizing substances.

Thus the hippuric acid of the urine might: (1) prevent formation of nuclei of stones by stabilization of the colloids; and (2) prevent secondary incrustation by its hydrotropic action. As a matter of fact, administration of sodium benzoate by mouth did: (1) prevent formation of stone in rats given a rich diet of calcium carbonate; (2) cause phosphaturia in man to disappear, and (3) diminish the attacks of renal colic among patients. Other more powerful stabilizers of the colloids in the urine (salicylates, mandelates) might be used for this purpose.

Function.—Habein and Mulrooney²⁸ stated that preservation and maintenance of adequate renal function is one of the most important considerations in the management of patients with lesions of the urinary tract. Functional disorders of the kidney associated with diseases of the urinary tract, which are often called "surgical" diseases of the kidney, differ etiologically, pathologically, therapeutically and prognostically from so-called medical nephritis. Hypertension and arterio-

27. Snapper, I., in discussion, Kong. d. internat. Gesellsch. f. Urol. 2:254-260, 1937.

28. Habein, H. C., and Mulrooney, R. E.: The Relation of Water, Sodium Chloride, and Acid-Base Balance to Renal Function in the Treatment of Lesions of the Urinary Tract, Am. J. Surg. 38:6-17 (Oct.) 1937.

sclerosis are not directly related to surgical diseases of the kidney, as is so often true in cases of glomerular nephritis.

Alterations in various components of the plasma may seriously affect renal function and retard its improvement. A knowledge of the physiologic mechanism of renal function is essential.

The maintenance of a proper water balance is one of the most important factors in complete renal function, and the modern use of fluids intravenously is one of the significant advances in medicine. That this method of supplying fluids parenterally is sometimes a life-saving measure cannot be doubted. There does not seem to be, however, a uniformity of opinion at present as to the amount and composition of intravenous solutions which should be used for various conditions.

Edema is not a frequent complication in surgical diseases of the kidney, but it may develop as a result of excessive intake of fluids, especially saline solution. The use of a 5 per cent solution of dextrose intravenously is probably preferable when fluids are to be given parenterally, unless there is a specific indication for other types of fluid.

The extrarenal causes of renal insufficiency, such as the toxemia associated with prolonged vomiting and obstructive lesions in the upper part of the gastrointestinal tract, play an important role in postoperative complications. Their role in renal insufficiency must be considered.

Lowering of the protein content of the plasma, when associated with malnutrition, anorexia and suppurative drainage, may occasionally be one of the factors in the production of edema.

The acid-base regulation of the plasma is an important consideration in maintenance or improvement of renal function. One of the nonexcretory functions of the kidney is the manufacture of ammonia. In the presence of renal insufficiency this mechanism is disturbed, and such disturbance results in acidosis. The treatment of acidosis associated with renal insufficiency by the use of intravenous alkalis, sodium lactate and lactate-Ringer solution was discussed.

ADRENAL TUMORS

Scholl²⁹ reported a case of tumor of the adrenal cortex. The patient was a young woman who came for treatment of high blood pressure, which had been about 200 mm. of mercury (systolic) for several months. For three years she had been gradually losing her hair, and recently it had become extremely thin. Eighteen months prior to examination her menstrual periods had ceased completely, after several months of lessened flow. During the last year she had noticed a growth of hair on her face, which she described at first as

29. Scholl, A. J.: Tumors of the Adrenal Cortex, *J. Urol.* 39:81-91 (Feb.) 1938.

"lanugo" but which at the time she was first seen was so thick and noticeable that it required periodic shaving. She had grown fleshy in the chest, the face and the neck. Physical examination showed increased adiposity of the face, the chest, the abdomen and the breasts. The blood pressure was 208 mm. of mercury systolic and 126 diastolic.

Cystoscopic examination revealed normal renal function. Pyelograms showed that each kidney was normally situated. Evidence of torsion, ptosis or extrarenal growth was not present. Bilateral exploration of both adrenal glands was made, and in the region of the left adrenal gland a pigmented, smooth, rounded, nonadherent mass about 4 cm. in diameter was found. This was removed. The opposite adrenal gland was small but apparently not abnormal.

After operation the blood pressure dropped rapidly in spite of injections of large amounts of saline solution, extract of adrenal cortex and epinephrine. The patient did not survive the operation.

Necropsy revealed that the remaining adrenal gland was greatly atrophied and that the small amount of renal tissue remaining on the left side, from which the tumor had been removed, had been destroyed by infarction. The pituitary gland and ovaries were not abnormal.

URETER

Injury.—Feiner³⁰ stated that it is likely that during the course of pelvic operation a certain number of unilateral ligations of the ureter occur, which are not recognized and do not provoke immediate symptoms but the ultimate result of which is that autonephrectomy occurs on the corresponding side. This accident may occur during any pelvic operation, but it is frequently associated with radical abdominal or vaginal hysterectomy and especially with operative procedures for the removal of intraligamentous tumors.

As an index of the seriousness of ureteral injury, the mortality figures cited by Bland, of 33.3 per cent for bilateral and 18.8 per cent for unilateral injury, may be mentioned.

The most frequent sequelae of ureteral injury are vaginal and abdominal fistulas. If a ligature or clamp has been placed on either one or both ureters, if the injury is detected at the time it is inflicted and if there is evidence that the vitality of the ureter has been so imperiled that a fistula is likely to develop, immediate repair should be done in the form of ureteroureteral or ureterovesical anastomosis. In the case of bilateral occlusion discovered after operation, with imminent danger of uremia, immediate deligation is the operation of choice, provided that the patient's condition is such that this hazardous and

30. Feiner, D.: *Operative Injuries of the Ureter*, Surg., Gynec. & Obst. **66**: 790-796 (April) 1938.

time-consuming operation can be endured. Nephrostomy may be the most feasible procedure when intra-abdominal procedures are contraindicated by the gravity of the patient's condition. If possible this drainage should be bilateral.

Feiner, in view of his results of 100 per cent mortality with 2 intra-abdominal deligations, concluded that nephrostomy with subsequent operation for ureteral anastomosis or vesical implantation is a much safer and therefore a preferable procedure.

Tumor.—Rusche and Bacon³¹ reported 2 cases of primary ureteral tumor, in 1 of which the growth was benign and in the other malignant. In each of these cases the tumor was diagnosed preoperatively by means of pyeloureterograms. A simplified method of obtaining pyeloureterograms was described, and it was suggested that this is an improvement in diagnostic procedure which will enable the only pathognomonic sign of ureteral tumor, the filling defect, to be visualized with less difficulty than formerly. A review of the literature on primary tumors of the ureter was included by these authors.

Ureteral Transplantation.—Farrell and Lyman³² presented an improved technic for ureterointestinal anastomosis. It differs from other technics in that after the usual incision in the bowel the submucosa is separated from the circular muscle at the lowest portion of the incision and is brought out through a small opening in the muscularis. A side to side anastomosis is then made between this tab of mucosa and the ureter, and a large silk suture is inserted to act as a sawing ligature to make the opening. This is done after a second line of suture brings the ureter and mucosa together above the first line, with the sawing ligature between. The ureter between the bladder and the anastomosis is then ligated and divided. (Farrell and Lyman considered this important because in the use of the ordinary transfixion suture with the ureter still attached to the bladder as in the Higgins operation, unless the urine is forced through the anastomotic opening immediately the opening tends to close. They said that the stoma closes if the ureter remains connected with the bladder for six to eight weeks.) The anastomosis is covered by interrupted sutures through the serosa and the muscularis in the usual manner.

This operation has the advantages of firmly uniting the bowel and the ureter before the stoma is made, thereby avoiding opening either the bowel or the ureter directly into the peritoneal cavity. However, the stoma is made immediately by the sawing ligature technic and is not

31. Rusche, C., and Bacon, S. K.: Primary Ureteral Neoplasms: Report of Two Cases and Review of the Literature, *J. Urol.* **39**:319-340 (March) 1938.

32. Farrell, J. I., and Lyman, Y.: Aseptic Uretero-Intestinal Anastomosis, *Surg., Gynec. & Obst.* **66**:657-662 (March) 1938.

dependent on the sloughing of a transfixion suture, with its temporary obstruction and its uncertainties. Likewise, the urine is forced through the stoma by ligation and division of the ureter distal to the opening, which assures its continued patency.

Studies of necropsies, including roentgenograms of 7 dogs which survived six months after this procedure, form the basis of Farrell and Lyman's conclusions.

The operation of ureterosigmoidostomy for diversion of the urinary stream has been accepted as the procedure of choice in cases of exstrophy of the bladder, irreparable vesicovaginal fistulas and intractable interstitial and tuberculous cystitis, as well as in selected cases of carcinoma of the bladder.

Nephrostomy, pyelostomy and ureterostomy as permanent creations have distinct disadvantages. With the advent of excretory urography it can be shown that the rectum serves adequately as a reservoir for urine and that the upper portion of the urinary tract is not damaged by transplantation of the ureters to the bowel. Therefore, this procedure should be adopted more frequently to permit total cystectomy for carcinoma of the bladder.

A wide variety of methods is available for treatment of tumors of the bladder, and the selection of the proper one will depend on the size of the tumor, its character (whether infiltrating or papillary), its position in the bladder and its grade of malignancy according to Broders' classification and whether single or multiple tumors are present.

The results of treatment are discouraging. Of 658 patients reported to the carcinoma registry of the American Urological Association, 45.9 per cent of patients who had tumors of grade 1 were alive after five years. Of patients with tumors of grade 2, 25.7 per cent remained alive after the same period; of patients with tumors of grade 3, 13.9 per cent, and of patients with tumors of grade 4, 4.3 per cent. Of this entire group, only 15.9 per cent were reported to be without evidence of cancer.

Most of the patients died of urinary obstruction with attendant urosepsis and uremia. The incidence of metastasis from carcinoma of the bladder is low, but because of encroachment on the ureteral orifices and secondary infection with pyelonephritis and hydronephrosis, 60 per cent of the patients died from renal causes.

Although total cystectomy preceded by ureterorectoneostomy has a limited application, Higgins³³ recommended it: (1) when the carcinoma is situated at the base of the bladder and the ureteral orifices are

33. Higgins, C. C.: Cystectomy and Transplantation of the Ureters into the Bowel for Carcinoma of the Bladder, *Surg., Gynec. & Obst.* **66**:549-556 (Feb.) 1938.

encroached on or the vesical sphincter is so involved that adequate local treatment would exert a destructive action on the ureteral orifice or would cause incontinence; (2) when extensive single or multiple infiltrating tumors are present; (3) when multiple, recurring tumors develop rapidly and cannot be controlled by fulguration, so that they eventually fill the bladder, and (4) when radical segmental excision of the bladder is not possible and it is believed that sufficient radium cannot be implanted for complete destruction of the tumor. Similarly, when a cystogram revealed evidence of much more extensive involvement of the vesical wall than was suspected on the basis of the cystoscopic picture, Higgins recommended the radical operation.

In addition to these four possibilities, certain other factors must be taken into consideration before the radical operation is recommended:

1. Renal function must be satisfactory, preferably in both kidneys but at least in one. In 3 instances Higgins has transplanted the ureter from the normal kidney into the bowel, finally performing the cystectomy after removing the opposite kidney because of infection and complete loss of function as the result of a vesical tumor obstructing the ureter.

2. The presence of metastasis or evidence of local extension of the malignant lesion must be taken into consideration. If at the time of transplantation of the ureters clinical evidence of extension of the carcinoma beyond the confines of the bladder is noted, Higgins concluded that the radical operation is inadvisable. Palpation of the regional lymph nodes and those at the bifurcation of the aorta is a routine procedure.

3. Intravenous urograms should be made to demonstrate that the caliber of the ureters is such that their implantation into the bowel is technically possible.

4. As Quinby has mentioned, demonstration of an actively growing carcinoma should be made by microscopic examination (biopsy).

Preoperative care should be governed by the following rules.

1. A liquid, nonresidual diet is supplemented by candy, dextrose and gelatin.

2. One thousand cubic centimeters of a 10 per cent solution of dextrose is administered intravenously each day. The dextrose is given with saline solution if renal function is not impaired, but if function is decreased, distilled water is substituted for the saline solution.

3. Magnesium sulfate is administered orally each day. One ounce (30 cc.) of magnesium sulfate is dissolved in 8 ounces (240 cc.) of water, 1 ounce of this mixture being taken every half hour, starting at 7 a. m. None, however, is used on the day prior to the operation.

4. The bowel is cleansed by a daily enema.

5. Provided there are no other complications, the number of days of preparation before operation depends on renal function and on the cleanliness of the bowel. When enemas return clear, the bowel is considered clean. On the day before the operation an enema is given both in the morning and at night.

6. Three doses of camphorated tincture of opium, each of 2 drachms (7.3 cc.), are prescribed at intervals of two hours, usually from 4 to 8 p. m. on the day before the operation.

7. Blood transfusions are used when indicated by the condition of the patient and that of the blood.

8. Complete study of the upper portion of the urinary tract is made by tests of function and by intravenous urographic study.

9. Urinary antiseptics are administered intravenously or orally as indicated.

10. Miscellaneous supportive measures are employed as necessary.

The Coffey I (Coffey-Mayo) operation is employed for patients who have impaired renal function or in the presence of varying degrees of dilatation of the ureters. The operation is done in two stages, followed by cystectomy. The Higgins modification of the transfixion suture technic is used when the ureters are of normal caliber and when renal function is only slightly impaired. The use of indwelling ureteral catheters (Coffey II) is unnecessary.

An exacting postoperative regimen is essential, and the following routine has given the most satisfactory results in Higgins' hands.

1. The patient is maintained in a supine position for at least eight hours if spinal anesthesia is used; then he is placed in Fowler's position.

2. The blood pressure is taken every fifteen minutes until it returns to normal.

3. Fluids are not administered by mouth for forty-eight hours, and then small amounts of water are taken orally for twelve hours. During the following twelve hours, clear fluids are given (1 ounce hourly), and this amount is gradually increased. A diet low in residue is then given for five to seven days.

4. The intake of fluid is maintained at 3,000 cc. daily. For the first two days, 2,000 cc. of 10 per cent solution of dextrose is administered intravenously and 1,000 cc. of saline solution is infused daily. After this period, fluids are given intravenously as indicated by chemical studies of the blood and by the amount of fluid taken by mouth.

5. Narcotics are given as necessary.

6. A rectal tube is inserted at the time of operation. This may be changed but is replaced and left in the rectum for eight to ten days. The rectal tube is irrigated gently at intervals of two to three hours to insure patency. When the transfixion suture technic is employed, gentle

traction is made on the rectal tube at the end of twenty-four, thirty-six and forty-eight hours until the tube containing the silk sutures is expelled. A plain rectal tube is then reinserted for five to seven days.

7. Chemical studies of the blood, i. e. determinations of the urea content and the creatinine content, are made daily until these concentrations return to normal.

8. Ten cubic centimeters of a mixture of methenamine and acetylaminosalicylic acid (a proprietary product called salihexin) is combined with the solution of dextrose given intravenously as a urinary antiseptic for the first three or four days after the operation.

9. General supportive measures are prescribed as indicated.

This careful preoperative and postoperative preparation reduces the incidence of peritonitis and acute renal infection. Improvements in technic have reduced the late complications, particularly obstruction and progressive hydronephrosis.

For 34 patients at the Cleveland Clinic, total cystectomy was preceded by ureterorectoneostomy. Insufficient time had elapsed at the time of the report to warrant statements as to the percentage of five year cures. The immediate results, however, were gratifying, and Higgins expressed optimism as to the future of this procedure.

Pain.—Ockerblad and Carlson³⁴ stated that the most common area in which ureteral pain occurs is in the lower quadrant, on or below a line drawn between the anterior superior spines of the ilium, halfway between the midline and the spines. On the right it is always inside, below McBurney's point and distinct from it. This point has been designated the focal point of ureteral pain.

Referred pain over the iliac crest has its origin in the upper portion of the ureter from the level of 26 to that of 28 cm. Immediate suprapubic pain has its origin in the terminal 1 or 2 cm. of the ureter. Genital pain, involving the labia or clitoris in the female and the penis and testicles in the male, has its origin most often in the lower third of the ureter.

Pain down the inner aspect of the thigh and leg is most frequent in the middle portion of the ureter or in the middle third, occurring from the level of 5 to that of 20 cm.

Renal pain is always in the back, at a point the center of which is the costovertebral angle, embracing a circular area about 8 to 10 cm. in diameter. Occasionally, ureteral pain may be referred to the anterior or lateral aspect of the thigh.

34. Ockerblad, N. F., and Carlson, H. E.: The Distribution of Ureteral Pain. *J. Urol.* 39:745-750 (June) 1938.

(To Be Continued)

OVARIAN DYSGERMINOMA

G. EMORY SEEGER, M.D.

BALTIMORE

The term dysgerminoma was introduced by Meyer to designate a rare type of ovarian tumor formerly referred to by a variety of names—seminoma, embryoma, sex cell carcinoma and large round cell sarcoma. A similar tumor occurring in the testis has been long recognized. Chenot in 1911 first called attention to the corresponding tumor in the ovary, although in this location its occurrence is far more infrequent. Chenot used the name seminoma because he considered the tumor to be derived from the anlage of the seminiferous tubules. Pick in 1912 described such a tumor as chorioepithelioma ectodermale; he concluded that it is teratoid and is derived from the cells of the chorionic villi. Meyer in 1925 made a comprehensive review of all the cases reported in the literature to that date and stressed that this tumor is the most frequent form found in the gonads of hermaphrodites and pseudohermaphrodites. Since the appearance of Meyer's paper many cases have been reported, the majority in the German literature. In the present paper 79 cases have been assembled from the literature, exclusive of 23 cases described by Meyer in which the patients were hermaphrodites or pseudohermaphrodites (table 1). Nineteen cases from the records of the Surgical Pathologic Laboratory are added (table 2).

No conclusions can be formed concerning the incidence of this type of tumor on the basis of the 19 cases, the present series, since these were not obtained from a routine gynecologic service. Klasten, from his studies of a series of 188 malignant ovarian tumors, estimated the incidence at about 3 per cent of all malignant ovarian tumors. Other observers have given an even lower frequency.

CLINICAL FEATURES

There are several clinical features which aid in arriving at a pre-operative diagnosis of dysgerminoma. These include the duration of symptoms and the age and sexual development of the patient. The

From the Surgical Pathological Laboratory, Department of Surgery and Gynecology, the Johns Hopkins Hospital and University.

TABLE 1.—*Summary of Seventy-Nine Cases Recorded in the Literature*

Author	Patient's Age	Site of Involvement	Metastases	Children	Condition	Treatment	Post-operative Course
Babes	13	Bilateral	+	0	Hypoplastic uterus	?	?
Bonnet	17	Left ovary	Ascites; recurrence	0	0	Excision of tumor	Ascites; recurrence at 3 mo.
Döderlein	19	Right ovary	+ Omental	0	Normal	Right salpingo-oophorectomy 1933; resection of omentum 1936	Living at 1 yr.
Du Pont	54	Left ovary	0	0	No right ovary	Excision of tumor	?
Dworzak	18	Bilateral	?	0	Normal	Bilateral salpingo-oophorectomy; hysterectomy	Dead at ½ yr.
Dworzak	20	Right ovary	+	0	Normal	Salpingo-oophorectomy	Dead at 13 days
Dworzak	44	Right ovary	?	1	Normal	Bilateral salpingo-oophorectomy; hysterectomy	Dead at 2 yr.
Dworzak	37	Left ovary	+	?	Normal	?	Dead at 1½ yr.
Fauvet	33	Right ovary	0	1	Normal	Right salpingo-oophorectomy	?
Fauvet	34	Bilateral	+	3	Normal	?	Dead
Fauvet	19	Left ovary	?	0	Amenorrhea; hypoplastic uterus; no right ovary	?	Dead
Fauvet	20	Left ovary	0	0	Normal	?	?
Fauvet	52	Bilateral	+	2	Normal	Bilateral salpingo-oophorectomy	Died
Fauvet	47	Bilateral	Recurrence with ascites 2 years	8	Normal	Bilateral salpingo-oophorectomy; hysterectomy; roentgen therapy	?
Frankl	28	Right ovary	+	0	No periods; undeveloped sexually	Bilateral salpingo-oophorectomy; hysterectomy	?
Frankl	51	Left ovary	0	0	Normal	Left salpingo-oophorectomy	?
Gilliard	19	Left ovary	+	1 p.o.	Normal	Left salpingo-oophorectomy; roentgen therapy	Living at 10 yr.
Gilliard	29	Bilateral	+	?	?	Laparotomy; roentgen therapy	Living at 1 yr.
Gross	25	Right ovary	?	1	?	?	?
Hajek	12	Right ovary	0	0	Uterus and ovary infantile	Hysterectomy; right salpingo-oophorectomy; roentgen therapy	?
Hajek	17	Right ovary	0	0	Normal	Bilateral salpingo-oophorectomy; hysterectomy; roentgen therapy	Living at 23 mo.
Hamman and Cornell	16½	Right ovary	0	0	Normal	Salpingo-oophorectomy	Well at 7 mo.
Hoehe	22	Right dermoid; left dysgerminoma	+	0	Normal	Right salpingo-oophorectomy May 1927; left salpingo-oophorectomy December 1927; roentgen therapy	Living at 3½ yr.
Keller	31	Bilateral	?	0	Hypertrophied clitoris; infantile uterus	?	?
Klatten	26	Bilateral	+	?	?	Bilateral salpingo-oophorectomy; hysterectomy	Dead at 2 mo.

TABLE 1.—*Summary of Seventy-Nine Cases Recorded in the Literature—Continued*

Author	Patient's Age	Site of Involvement	Metastases	Children	Condition	Treatment	Post-operative Course
Klaften	23	?	+	?	?	?	?
Klein	15	Right ovary	0	?	Normal	?	Dead at 5½ yr.
Klein	15	Left ovary	0	0	Normal	Bilateral salpingo-oophorectomy; hysterectomy	?
Klein	19	Right ovary; left ovary 2 years later	?	0	?	Right salpingo-oophorectomy; left salpingo-oophorectomy	Dead
Klein	24	Right ovary	0	0	Sterility	Extirpation of tumor; roentgen therapy	Living at 16 yr.
Klein	22	Left ovary	0	2 post-operatively	Periods in menarche 18 yr.	Right salpingo-oophorectomy	Living at 7 yr.
Klein	30	Bilateral	0	1	Normal	Bilateral salpingo-oophorectomy	Living at 1½ yr.
Klein	17	Left ovary	0	0	Amenorrhea 4 mo.	?	Living at 4 mo.
Laffont and Bonafos	21	Right ovary	+ Aseites	1	Normal	?	Died at 4 mo.
Lubarsh	13	Bilateral	+	0	No periods	None	Dead
Matsner	33	Right ovary	0	0	Hypoplastic uterus; aplastic ovary; no periods	?	Died at 18 days
Matsner	17	Right ovary	Aseites	0	Irregular periods	Bilateral salpingo-oophorectomy	Well at 1 yr.
Matsner	25	Right ovary; left ovary 6 mo. later	+	0	Normal	Right salpingo-oophorectomy 1923; left salpingo-oophorectomy 1924; hysterectomy	?
Masson and Desmarest	14	Left ovary	+	0	No periods	Salpingo-oophorectomy	Died at 48 hr.
Ménétrier, Peyson, Isch-Wall and Lory	45	Right ovary	0	0	Clitoris enlarged; left ovotestis; cord for uterus	Bilateral salpingo-oophorectomy	Well
Ménétrier, Peyson, Isch-Wall and Lory	54	Left testicles undescended	0	0	Pseudohermaphrodite	Excision of tumor; successfully treated by roentgen therapy 6 yr. later	Recurrence 6 yr. ago; well at 12 yr.
Meyer	15	Bilateral	0	0	Normal	Bilateral salpingo-oophorectomy	Living at 6 yr.
Meyer	16	Right ovary	0	0	Hypoplastic uterus; normal periods after operation	Right salpingo-oophorectomy	Living at 8 yr.
Meyer	28	Left ovary	0	0	Hypoplastic uterus; regular periods	Left salpingo-oophorectomy	Living at 4 yr.
Meyer	40	Left ovary	Liver	0	Never menstruated	Extirpation of tumor	Dead at 2 yr.
Meyer	16	Right ovary	?	0	Aplasia of ovary and uterus; no menstrual periods	Laparotomy	?
Meyer (Marion)	36	Right ovary	?	0	Pseudohermaphrodite	Extirpation	?
Meyer	30	Right ovary	0	0	Left ovotestis	Exploratory laparotomy	?
Neumann	15	Right ovary	?	?	?	?	?
Neumann	22	Right ovary	0	0	Hypoplastic uterus	Right salpingo-oophorectomy	Living at 6 mo.
Neumann	22	Bilateral	0	0	Normal	Bilateral salpingo-oophorectomy	?
Pick	9	Right ovary	+	0	Normal	0	?

TABLE 1.—*Summary of Seventy-Nine Cases Recorded in the Literature—Continued*

Author	Patient's Age	Site of Involvement	Metastases	Children	Condition	Treatment	Post-operative Course
Reifferscheid	35	Right ovary	0	3 abortions	Normal	?	?
Reifferscheid	18	Right ovary	0	0	Normal	?	Well
Reifferscheid	17	Bilateral	0 Ascites	0	Normal	?	?
Reifferscheid	14	Left ovary	+	0	Normal	Roentgen therapy	Well at 4 mo.
Reifferscheid	20	Right ovary	0	0	Normal	?	Well at 2 yr.
Reifferscheid	19	Left ovary	0	0	Normal	Bilateral salpingo-oophorectomy	Well at 3 yr.
Rössle	10	Bilateral	+	0	Normal	?	?
Schiller	13½	Bilateral	0	0	Normal	Bilateral salpingo-oophorectomy; hysterectomy	Living at 8 yr.
Schiller	28	Bilateral	+	0	Infantile genitalia	Bilateral salpingo-oophorectomy; roentgen therapy; hysterectomy	Living at 2 mo.
Schiller	18	Right ovary	0	0	Irregular periods	Roentgen therapy	?
Schiller	18	?	0	0	?	?	?
Schiller	24	Bilateral	0	2	Normal	Laparotomy; roentgen therapy	Well
Schiller	16	Right ovary	0	1 p.o.	Normal	Right salpingo-oophorectomy	Living at 10 yr.
Schiller	14	Bilateral	0	0	No periods	Bilateral salpingo-oophorectomy; hysterectomy; roentgen therapy	Living at ½ yr.
Schiller	19	Right ovary	0	1 p.o.	Normal	Right salpingo-oophorectomy	Living at 2 yr.
Schiller	47	?	?	3	Normal	?	?
Schiller	65	?	?	1	Normal	?	?
Szathmáry	28	Right ovary	Infiltration, rectum	2	Normal	Bilateral salpingo-oophorectomy; hysterectomy	?
Szathmáry	17	Right ovary	0 Ascites	0	Normal; amenorrhea 3 mo.	Left salpingo-oophorectomy	Well at 9 yr.
Szathmáry	22	Left ovary ?	Infiltration, omentum	0	Normal	Exploratory laparotomy	?
Szathmáry	36	Right ovary	0	5	Normal pregnancy present	Right salpingo-oophorectomy	Well at 4 mo.
Szathmáry	20	Bilateral	Infiltration	1	Tuberculosis	Bilateral salpingo-oophorectomy; hysterectomy	?
Tietze	10	Left ovary	0	0	Two periods; ceased after extirpation	Left salpingo-oophorectomy	Living at 1 yr.
Walls	17	Left ovary	0	0	Normal	?	Living at 4 wk.
Wolfe and Kaminester	13	Right ovary	+	0	Normal	Exploratory laparotomy	Died at 4 days
Zacharias	32	Undescended right testis	?	0	Female hermaphrodite	?	?
Zimmerman	17	Left ovary	0	0	Amenorrhea; normal periods after operation	Left salpingo-oophorectomy	Living at 1½ yr.
Zucker	26	?	+	0	Male hermaphrodite	?	Dead

TABLE 2.—*Summary of Nineteen Cases from the Records of the Surgical Pathologic Laboratory*

Patient	Age	Involvement	Metastases	Children	Condition	Treatment	Post-operative Course
20147	14	Left ovary	0	5 p.o.	Periods irregular 1 year, otherwise normal	Left salpingo-oophorectomy	Well at 20 yr.
15920	19	Right ovary	+ Bladder and rectum	0	Underdeveloped infantile uterus and left ovary; no periods	Bilateral salpingo-oophorectomy; hysterectomy	Dead at 11 mo.
37014	26	Left ovary	+ Recurrence	1	Normal	Left salpingo-oophorectomy; roentgen therapy	Well at 12 yr.
40452	13	Both ovaries	0	0	Normal	Bilateral salpingo-oophorectomy; hysterectomy	Well at 8 yr.
47822	39	Right testis	+ Recurrence	0	Male pseudo-hermaphrodite; no ovaries; testis undescended; tubes and uterus	Bilateral salpingectomy; hysterectomy; excision of tumor; roentgen therapy	Well at 5 yr.
57044	12	Right ovary	0 Ascites	0	?	Right salpingo-oophorectomy	Living at 4 mo.
57440	35	0	10	Normal	Excision of tumor; roentgen therapy	Living at 2 yr.
57544	18	Right ovary	0	0	Normal	Right salpingo-oophorectomy	Well at 4 mo.
.....	26	Left ovary	0	0	Normal	Left salpingo-oophorectomy; suspension of uterus; appendectomy	Well at 7 yr.
57550	23	Right ovary	0	0	Underdeveloped; amenorrhea 6 years; periods irregular at first	Exploratory laparotomy	Died at 4 days
57738	22	Right ovary	0	0	Advanced tuberculosis	Autopsy	Died from tuberculosis
46868	30	Right broad ligament	0 Recurrence	0	Female pseudo-hermaphrodite with reversion	Excision of tumor; roentgen therapy to recurrence	Died after 3 yr. from lobar pneumonia
32313	12	Right broad ligament	0	0	Normal	Excision of tumor; appendectomy	Well at 7½ yr.
57760	13	Right ovary	0	0	Normal; periods normal after operation	Right salpingo-oophorectomy	Living at 2 yr. 10 mo.
57960	34	Right ovary	0	1	Normal	?	?
58018	22	?	0	0	Normal	?	?
53016	31	Both ovaries	+	?	Normal	Laparotomy	Died at 1 mo.
57578	14	Left ovary	+ Uterus	0	Dysmenorrhea 4 mo.	Left salpingo-oophorectomy; roentgen therapy	Dead at 4 yr.
56320	28	Right ovary	+ Pancreas, liver, spleen, omentum, ascites	0	Normal	Right salpingo-oophorectomy	Died at 1 mo.

occurrence of a large, solid tumor in the right ovarian region in a girl past puberty is suggestive of such a diagnosis. The duration of abdominal pain and swelling (which are the leading symptoms) is usually about six months. Meyer has laid stress on the occurrence of dysgerminoma with pseudohermaphroditism, hypogenitalism and other forms of sexual maldevelopment, such as infantilism, amenorrhea, delayed onset of menstruation and sterility. The absence of such abnormalities, however, is of no diagnostic significance. In 50 cases collected from the literature the tumor occurred in an otherwise normal person. Fifteen of 19 patients in the cases here reported had apparently normal external genitalia and secondary sexual characteristics. One showed infantilism, 2 were pseudohermaphrodites and another had amenorrhea. Patients with dysgerminoma are usually under 30 years of age; in the majority of cases in this series the tumor occurred while the patient was under 20 (table 3). This age distribution does not seem to apply in hermaphrodites and pseudohermaphrodites. Such patients are older. Dysgerminoma (seminoma) in the testis is most frequent after the age of 30 (Ferguson).

On palpation of the abdomen a tumor may be felt, which on pelvic examination gives the impression of a hard or elastic mass with an irregular nodular surface. Roentgenograms of the pelvis occasionally prove of value in differentiating such a tumor from a dermoid cyst or teratoma containing calcareous material.

Extensive infiltration of the rectum or the bladder with involvement of the retroperitoneal lymph nodes occurs with the more malignant tumors; however, metastasis to other organs is rare. In only 2 cases found in the literature was there metastasis elsewhere, in 1 case to the kidney and in the other to the liver. Ascites occurs in a small number of cases. In case 18 of the present series metastases were found in the spleen, the pancreas and the kidney. Metastasis to the lungs has not been reported.

Several observers have recently reported the presence of gonadotropic substances in the urine of patients with this type of ovarian tumor. However, quantitative assay has seldom been reported, and when the value has been given it has been under 200 rat units per liter. Wallis reported 150 to 200 mouse units per liter. Ferguson has reported higher values, 400 to 20,000 mouse units per liter, in 10 cases of seminoma of the testicle. The small amounts present in the urine and the rarity of the cases of ovarian dysgerminoma in which this test was performed make such a test of doubtful diagnostic value. In the case of Wallis the value was only slightly higher than that found at times in the urine of castrated persons or in urine obtained during the menopause.

No determinations have been made to indicate that the tumor itself secretes an endocrine substance. Assays on tumor tissue were found negative for gonadotropic substance by Zondek. He was unable to demonstrate any significant hormonal output in the urine of a patient with such a condition. In case 17 in the present series an Aschheim-Zondek test performed on the urine gave a negative result. Such assays should be carried out in all cases of suspected ovarian tumor, as only in this way will sufficient data be obtained to determine the significance of this test. Other endocrine studies, particularly assays of the blood and urine for estrogen, would be of interest because of the frequent associations of such tumors with sexual maldevelopment. In cases in which menstrual disturbances are present, low values for estrogen might be disclosed. The results of assays for androgen would be of interest also in cases in which the tumor is associated with hermaphroditism or pseudohermaphroditism.

TABLE 3.—*Age Incidence*

	Age					Total Cases
	0 to 9	10 to 19	20 to 29	30 to 39	40+	
Cases (Surg. path. lab.).....	0	8	6	5	0	19
Cases (literature).....	2	35	22	12	8	79
	2.5%	44.5%	28%	15%	10%	

PATHOLOGY

The outstanding gross pathologic features of this tumor are the firm or elastic consistency, the nodular surface and the large size (often in excess of 2,000 Gm.), suggesting rapid growth (fig. 1). The cut surface is granular and glistening, and the more dense stromatogeneous areas are widely separated. Microscopically the cells of the tumor stand out individually, suggesting the appearance of caviar, especially in the frozen section, in which phenomena of fixation play no part. The cells are large and discrete; they are arranged in nests and strands, with a moderate amount of clear cytoplasm which takes the eosin stain and with large hyperchromatic nuclei. In the better preserved cells nucleoli are a prominent feature. These features are well emphasized in figure 2. A characteristic arrangement in nests and strands is produced by the stroma, which forms a delicate network separating each cell and group of cells. With proper staining technic relatively large amounts of glycogen may be demonstrated in the cytoplasm (Döderlein). One of the more constant characteristics of the microscopic structure of these growths is the lymphoid infiltration of the stroma. The lymphoid nature of these cells, however, has not been fully established. Their minute size, the density of the chromatin in

them and the relative absence of cytoplasm suggest extruded polar bodies. The appearance of pseudotuberculosis, described by Schiller in 1936, was not present in the cases recorded in the surgical pathologic laboratory. In the present series of 19 cases the histologic picture has been uniform, unmixed with that of other types of tumor except in case 19. However, in 4 cases among those reviewed in the literature there was follicular arrangement resembling that of the granulosa cell tumor. Two of these cases were reported by Schiller, 1 by Reifferscheid and 1 by Babes. In a case reported by Hoche in 1930 the tumor was associated with a dermoid cyst, and in a case reported by Hartmann, Ménétrier and Isch-Wall dysgerminoma of the testis was associated with chorioepithelioma. In 3 cases which will be reported from the gynecologic service of the Johns Hopkins Hospital, there was a combination of dysgerminoma with malignant teratoma.

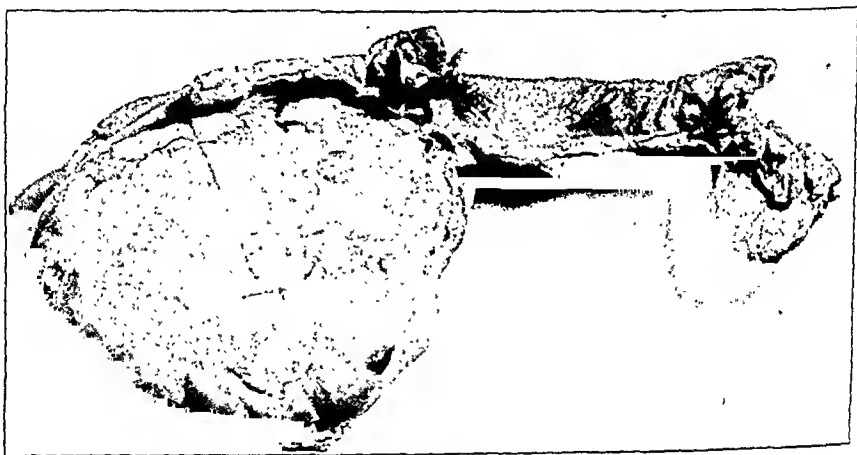


Fig. 1 (case 5).—Gross specimen of dysgerminoma occurring in a pseudo-hermaphrodite. Fallopian tubes, uterus and testes are present but there is no ovarian tissue outside the tumor. The patient is well five years after operation. For photomicrograph see figure 9.

In case 19 the bulk of the tumor was composed of primitive vascular tissue containing large cells, sometimes of epithelial appearance, with occasional giant cell formation and in other places containing spindle cells, such as those found in mesothelioma of the pleura (figs. 3 *A* and 3 *B*). Whether this tumor should be regarded as an example of dysgerminoma associated with chorioepithelioma, as reported by Hartmann, Ménétrier and Isch-Wall in a case of testicular tumor, or as a combination of dysgerminoma with a malignant tumor arising from undifferentiated elements of the ovarian stroma is not certain.

Malignant tumors of the retroperitoneal spaces, containing large cells suggesting those seen in dysgerminoma but with greater variation

in size and in staining reaction of both nucleus and cytoplasm, have been described. These tumors may also contain lymphoid stroma. It has been suggested by Schiller that such a tumor may be an ectopic dysgerminoma. However, such possible malignant variants cannot be properly classified with any degree of assurance, and they have been excluded from the present series.

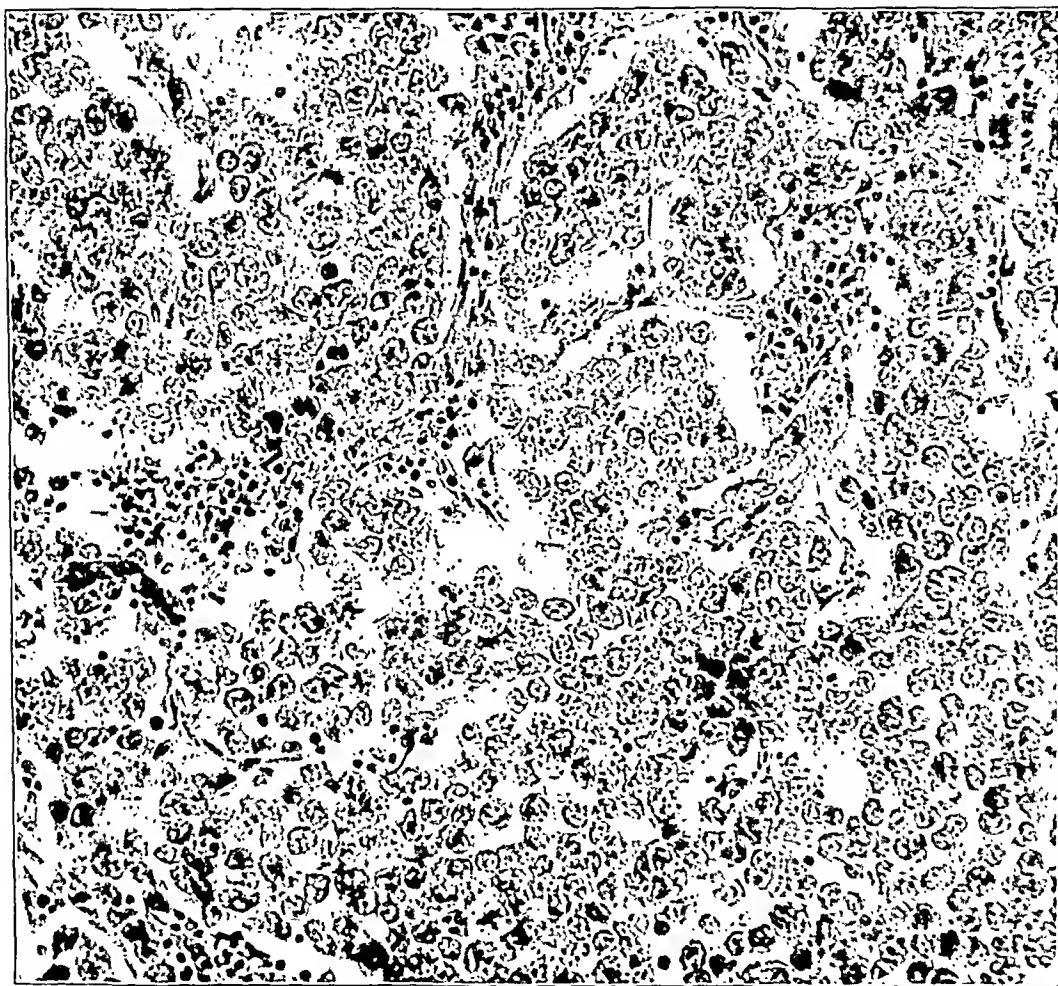


Fig. 2 (case 2).—Photomicrograph of a typical dysgerminoma, showing the caviar-like cells and lymphoid stroma. The tumor tissue is divided into nests or islands by delicate strands of connective tissue.

Uncertainty in regard to classification also applies to so-called senile dysgerminoma. This term has been applied to solid ovarian tumors containing cells resembling those found in typical dysgerminoma but without lymphoid stroma and occurring in elderly patients. Their atypical microscopic appearance and their occurrence in patients of advanced age have been attributed to slow and asymptomatic growth

over many years, which allows the tumor to remain latent and undiagnosed. Such an interpretation seems paradoxical, however, in view of the malignant clinical behavior of some of the tumors thus classified. Attempts to enlarge the dysgerminoma group by inclusion of histo-

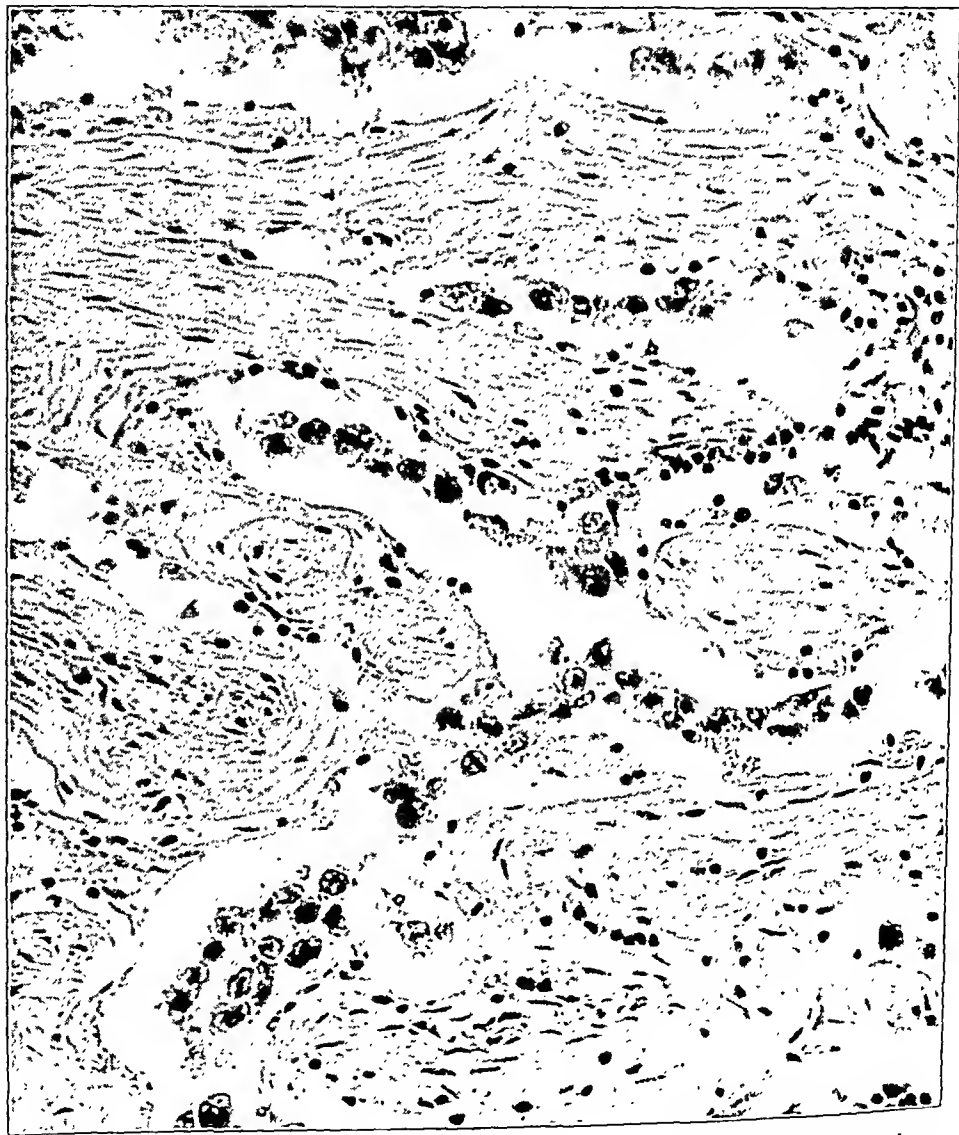


Fig. 3 A (case 19).—Photomicrograph of a complex dysgerminoma, showing the histologic character of typical dysgerminoma.

logically atypical tumors can only lead to confusion, and in the present study all such histologic variants have been carefully excluded.

PROGNOSIS AND TREATMENT

The prognosis in cases of dysgerminoma is much disputed. On one hand, Meyer said the tumor is relatively benign, and on the other,

Klaften reported it as an "exquisite malignancy." This difference of opinion is partly due to the small series of cases reported by individual observers and the still smaller series of cases followed and partly due to the impossibility of differentiating the benign from the malignant

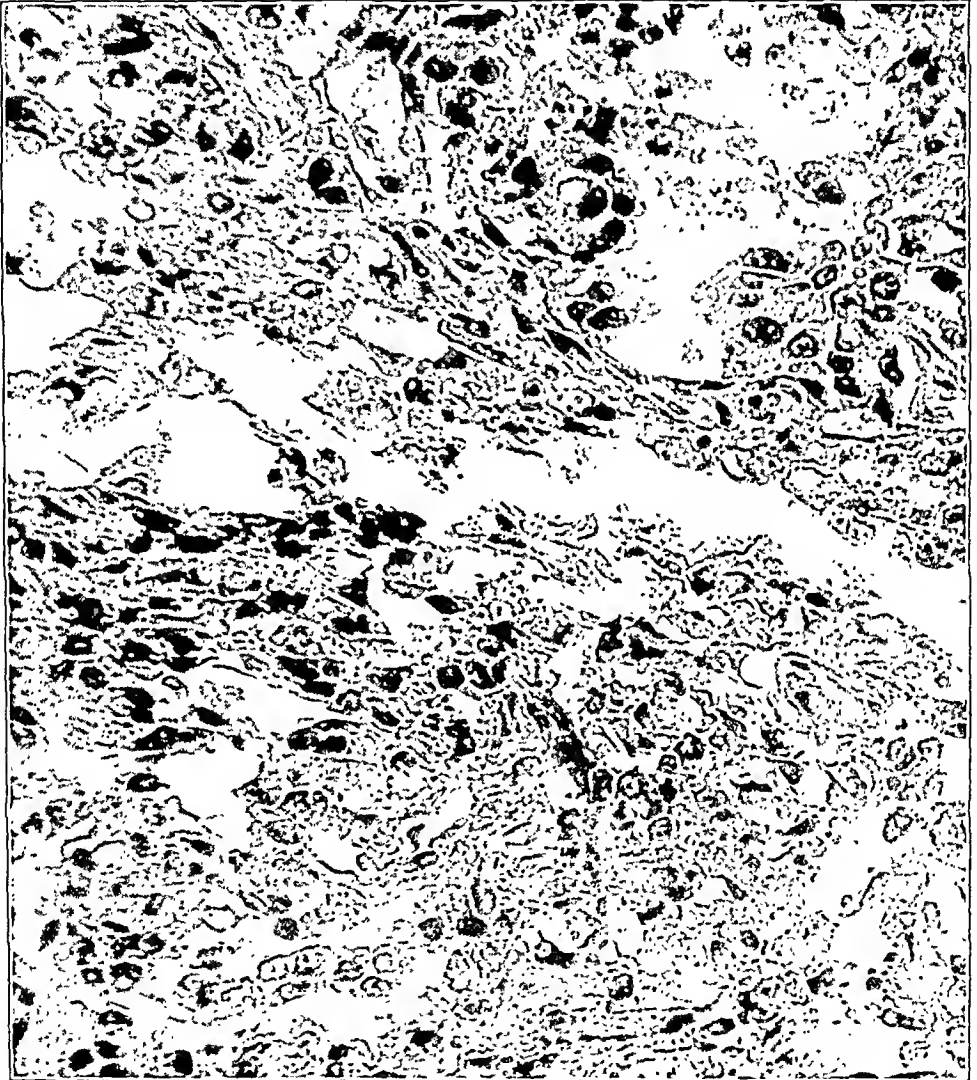


Fig. 3 *B*.—Photomicrograph showing the histologic character of another area of the tumor shown in figure 3 *A*, in which a mixture of large spindle cells and malignant epithelial cells suggests sarcoma of undifferentiated ovarian stroma or possibly chorionic tissue.

forms microscopically, a difficulty which is found frequently with all types of ovarian tumor. Fauvet, however, claimed to be able to give a correct prognosis on the basis of three criteria: (1) tumors found

at operation to be infiltrative and not discrete or associated with lymphatic metastasis are malignant; (2) the malignant tumor histologically shows extreme cellularity and paucity of connective tissue, and (3) the urine of patients with malignant dysgerminoma will give a positive reaction for gonadotropic substance.

Fauvet's first criterion is the most reliable, for in 17 cases of metastatic tumor reviewed in the literature in which the course of the process was adequately followed, 10 patients died, 6 were living after less than five years and only 1 was living after more than five years. In 4 of 7 cases of tumor with metastasis to the lymph nodes recorded in the surgical pathologic laboratory the growth was noted at operation to be infiltrative and the patient died. The patient in 1 of these cases (case 18) died in spite of roentgen therapy. In the other 3 cases there were recurrences in the lymph nodes after operation. In 1

TABLE 4.—*Lack of Correlation Between Clinical Results and Degree of Malignancy as Determined by Number of Mitoses*

Case No.	Number of Mitoses in 40 High Power Fields	Results
17	11	Died 1 month after operation
18	17	Died 4 years after operation
5	19	Well 5 years after operation
12	23	Died 3 years after operation, from lobar pneumonia
2	37	Died 11 months after operation
15	41	Not traced
11	41	Died from tuberculosis
14	41	Well 2 years and 10 months after operation
1	46	Well 20 years after operation
4	46	Well 8 years after operation
10	48	Died 4 days after operation
19	49	Died 1 month after operation
3	50	Well 12 years after operation
13	71	Well 7½ years after operation

of these complete cure followed postoperative roentgen therapy, and at the time of writing the patient has remained well for twelve years. In another the growth was arrested by implantation of radon; the patient was living and apparently well five years later. In the third case the condition responded to roentgen therapy; the patient lived three years, finally succumbing to lobar pneumonia.

In my experience, the degree of microscopic differentiation cannot be relied on in distinguishing a benign from a malignant tumor. The appearance of gonadotropic substance in the urine is likewise unreliable as a guide to prognosis, because of the scarcity of such determinations reported to date.

In 14 cases in the present series an attempt was made to distinguish benign from malignant dysgerminoma by counting the number of mitotic figures in forty successive high power fields (table 4). The results of these counts show that there is no correlation between the frequency of mitotic figures in the sections and the degree of malignancy of the tumor as shown by follow-up reports (figs. 4 and 5).

Of the cases in which there were adequate follow-up data, the patients in approximately 50 per cent have remained well beyond five years. Of 17 cases in which death was reported in the literature, in 5 it was postoperative and in 12 apparently from the effects of the tumor. Of 33 patients reported in the literature as living, only 10 were followed beyond five years. Of 19 patients studied by me 6 were living after five years, 4 were living under five years and 4 were dead from metastasis. Of the 4 remaining patients, 2 died from causes other than tumor, and 2 have not been traced (table 5).

The treatment of choice for dysgerminoma is excision of the tumor, the uterus and the opposite ovary being left intact. The preservation of the child-bearing function is desirable for the patients, who are usually young adults. For patients showing hermaphroditism or sexual underdevelopment the possibility of future pregnancy is usually a consideration of no importance. For patients showing recurrence of the tumor in the regional lymph nodes after a primary excision, irradiation or a second excision is indicated.

TABLE 5.—*Mortality*

	Dead			Alive		
	Post-operative Deaths	Deaths from Tumor	Deaths from Other Causes	Under Five Years	Over Five Years	Not Traced
Cases (Surg. path. lab.).....	1	4	2	4	6	2
Cases (literature).....	5	12	?	23	10	29

In the advocacy of conservative surgical treatment for dysgerminoma the possibility of recurrence of the tumor in the opposite ovary must be considered. Only 2 cases of such involvement have been recorded in the literature. On the other hand, in 6 cases in which the affected ovary only was removed (5 reported by other authors and 1 in my own series) the patient subsequently gave birth to a healthy child. This would seem to warrant the slight risk of recurrence in the opposite ovary which is assumed when conservative excision is practiced.

Dysgerminoma of the ovary ranks with myeloid and lymphoid tumors in its radiosensitivity. Several authors, Gilliard (1 case) and Ménétrier, Peyron and others (2 cases), have reported the rapid disappearance of large metastatic masses after external irradiation. It is interesting to note that both surgical and roentgen treatment are far more successful in cases of dysgerminoma of the ovary than in cases of testicular tumor of an identical histologic composition.

In cases in which complete removal of the tumor cannot be accomplished, irradiation is the only effective method of treatment. Irradiation for recurrences in the lymph nodes resulted in ultimate cure in 3 cases in the present series. In 1 of these (case 3) there was a

recurrence in the retroperitoneal nodes one and one-half years after the primary operation. The patient received repeated courses of high voltage roentgen therapy during five years and at the time of writing has remained well for twelve years after the operation. In the second



Fig. 4 (case 1).—High power photomicrograph showing the apparently malignant histologic composition of the tumor, with numerous mitotic figures. This patient with dysgerminoma remained well twenty years after the operation. Compare with figure 5.

case (case 5) the condition was treated by implantation of radon seeds into a recurrent tumor mass in the right lumbar region. The patient has remained well more than five years. In a third case (case 12)

the patient's condition was much improved after high voltage roentgen therapy. She was apparently free of tumor three years later, at which time death occurred from pneumonia.

HISTOGENESIS

The histogenesis of dysgerminoma of the ovary is not yet established. The most widely accepted theory at present is that of Meyer,

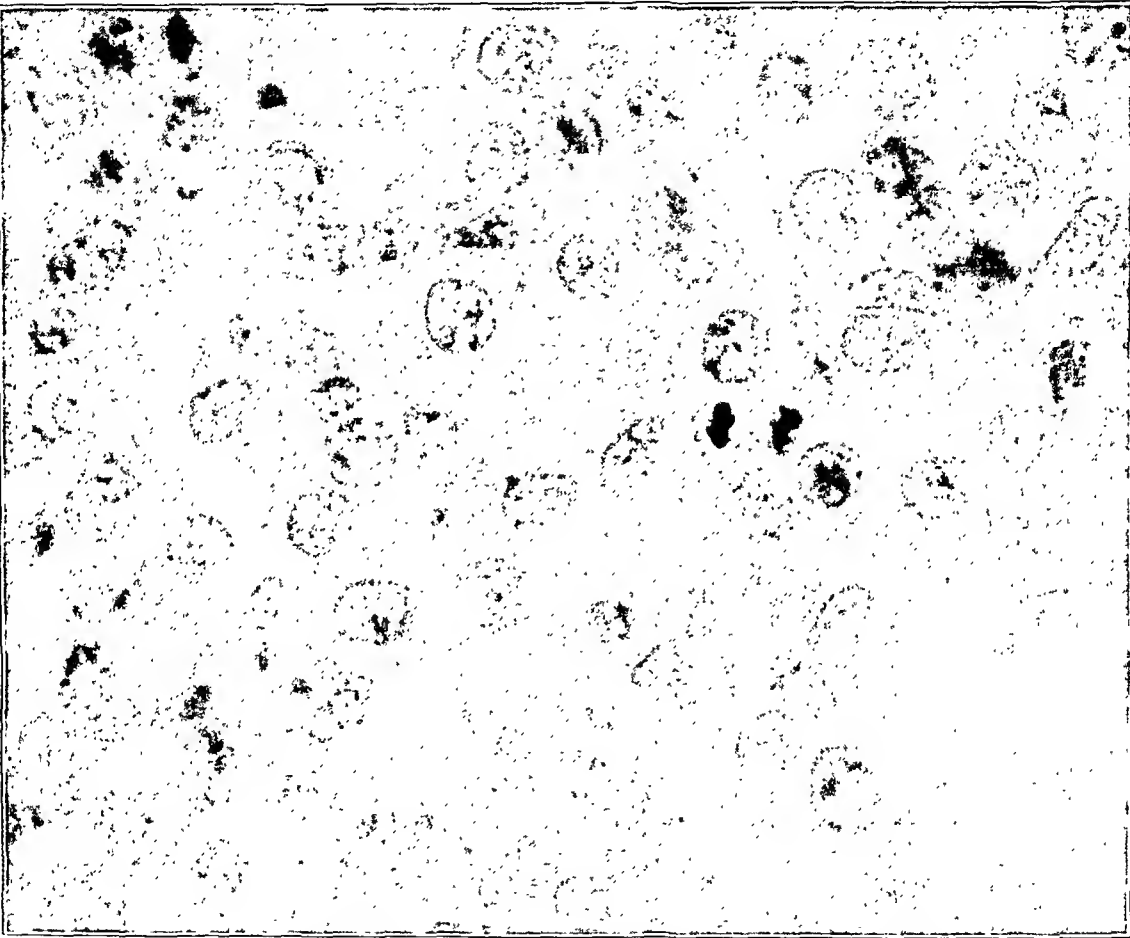


Fig. 5 (case 2).—High power photomicrograph of an ovarian dysgerminoma similar in histologic composition to that in case 2 (fig. 4). This tumor infiltrated the bladder and the retroperitoneal lymph nodes. The patient died eleven months after the operation.

who concluded that the tumor cells are derived from indifferent germ cells of the genital ridge. He stated the belief that such an origin from indifferent germ cells which retain the power to produce both the male and the female gonads accounted for the common occurrence of such tumors in hermaphrodites. It would also account for the occur-

rence of dysgerminoma tissue in cases of teratoma of the ovary and chorioepithelioma of the testis, reported in the literature. Meyer stated that the occurrence of dysgerminoma in otherwise normal women is against the view of Chenot, who concluded that the tumor is derived from the cells of the testicular anlage in the woman. However, since each female gonad passes through a stage corresponding to that of the male, thus making every female temporarily a potential hermaphrodite, it is impossible to say that somewhere in the ovaries of apparently normal women there is not a small focus of male anlage remaining, which gives origin to dysgerminoma. Moreover, the fact that the tumor is about three times as common in the testis as in the ovary seems to favor such an origin.

One observation bearing on the histogenesis of dysgerminoma is its predilection for the right ovary. In 48 per cent, or 35, of the cases reviewed the tumor occurred in the right ovary, while in 26 per cent, or 19, the condition was bilateral. Only 26 per cent of the tumors arose from the left ovary. Of these, 2 occurred in patients who had no right gonad (table 6). This is significant when viewed embryologically, for

TABLE 6.—*Location of Tumor*

	Location		
	Right Ovary	Left Ovary	Bilateral
Cases (Surg. path. lab.).....	11	4	2
Cases (literature).....	35 (48%)	19 (26%)	19 (26%)

the right ovary develops more slowly and to a lesser degree than does the left ovary. Also, from the standpoint of comparative anatomy it is known that in birds the right ovary remains undeveloped throughout life. Thus, if undifferentiated tissue remains behind, the probability of its occurrence in the right ovary is greater than in the left, and if the tumor is derived from such embryonic tissue, which seems to be the case, it is not surprising that it occurs more frequently in the right ovary. The following cases are from the records of the laboratory of surgical pathology.

REPORT OF CASES

CASE 1 (Dr. J. King B. E. Seegar, Baltimore).—L. S., a girl aged 14, was admitted to the hospital because of violent pain in the left side of the abdomen, accompanied with nausea and vomiting of one day's duration. The menstrual periods had begun at the age of 13 and were still irregular. The last period occurred two months previous to the onset of the present illness. Examination of the abdomen showed rigidity in the lower left quadrant, with marked tenderness. Pelvic examination showed normal external genitalia. The uterus was small and was pressed backward. To the left there was a large irregular mass occupying the lower part of the abdomen, anterior to the uterus. A clinical diagnosis of ovarian cyst with twisted pedicle, probably a dermoid, was made, and operation was performed immediately. The tumor involved the left ovary and had a twisted

pedicle. It was completely free, with no points of adhesion. The tumor and the left tube and ovary were removed. The other pelvic organs were normal. On gross examination the tumor was seen to be the size of a child's head. It was solid and grayish and had an elastic feel. The impression from the gross specimen was that the tumor was a sarcoma. The microscopic picture was typical of dysgerminoma. A follow-up report in November 1936, twenty years after the operation, stated that the patient is well and has five children.

CASE 2 (Dr. J. King B. E. Seegar, Baltimore).—E. S., a woman aged 19, entered the hospital with the complaint that she had never menstruated. There had been frequent voiding of urine and nocturia of increasing severity during the past year. Physical examination revealed a poorly nourished woman with a hard, nodular mass palpable in the abdomen, filling both lower quadrants and reaching to the renal area on the right. The pelvic examination showed normal external genitalia and a hard nodular mass filling the entire cul-de-sac, pushing the small uterus far to the right. The rectal examination showed enlarged retroperitoneal glands. At operation the mass, which arose from the right ovary, completely filled the pelvis and infiltrated the bladder. The iliac and retroperitoneal glands were involved. There were a large tumor about the right kidney and questionable infiltration of the rectum. The uterus was infantile, and the left ovary was only 1 cm. in diameter. The large tumor was extirpated; bilateral salpingo-oophorectomy and hysterectomy were performed. Grossly the tumor mass was seen to be about 15 cm. in diameter and was firm. On section the tissue was coarsely granular, with widely separated fibrous septums. The microscopic diagnosis at the time was carcinoma of the ovary. Reclassification of the tumor showed it to be a dysgerminoma (fig. 6). The patient died eleven months after the operation.

CASE 3 (Dr. Joseph C. Bloodgood, Baltimore).—S. E., a white woman aged 26, married, had one child aged 1 year. The menstrual history was normal. She complained of vague abdominal distress, and on physical examination a large, firm tumor in the lower part of the abdomen was found, which apparently arose from the left ovary. At operation a large, freely movable tumor of the left ovary was removed; the right ovary was normal. The diagnosis was large round cell sarcoma, and the patient was given roentgen treatments in November 1923 and in January 1924. On reclassification this tumor was found to be a dysgerminoma (fig. 7). In May 1925 there was a recurrence. A second laparotomy revealed involvement of the retroperitoneal glands by tumor tissue microscopically similar to that found at the time of the first operation. Thereafter the patient received irradiation treatments every six months until 1930. In June 1930 the mass had completely disappeared, and the patient was asymptomatic. The patient was reported well in June 1935, twelve years after the date of the first operation.

Although at operation this tumor was apparently benign, as judged by complete mobility and absence of infiltration, there was widespread recurrence. The response of the recurring tumor to irradiation suggests that frankly malignant tumors, such as that in case 2, should also respond to such therapy.

CASE 4 (Dr. J. Wainwright, Scranton, Pa.).—M. S., a girl aged 13, complained of pain in the lower part of the abdomen one week prior to admission. The menstrual periods had begun at the age of 12 and had been regular. On physical examination a large tumor was found in the lower part of the abdomen, and an exploratory laparotomy revealed bilateral ovarian tumor. Bilateral salpingo-oophorectomy and hysterectomy were performed. On gross examination the tumors were seen to be firm, solid and whitish and to have irregular surfaces. The microscopic diagnosis was bilateral dysgerminoma (fig. 8). The patient was

20 years of age when last heard from, Dec. 29, 1936, seven years and ten months after the operation. She was in excellent health, and there was no evidence of metastasis.

CASE 5 (Dr. V. Norwood, Baltimore).—B. P., a man aged 39, a pseudohermaphrodite, complained of nausea, vomiting and pain in the right lower quadrant

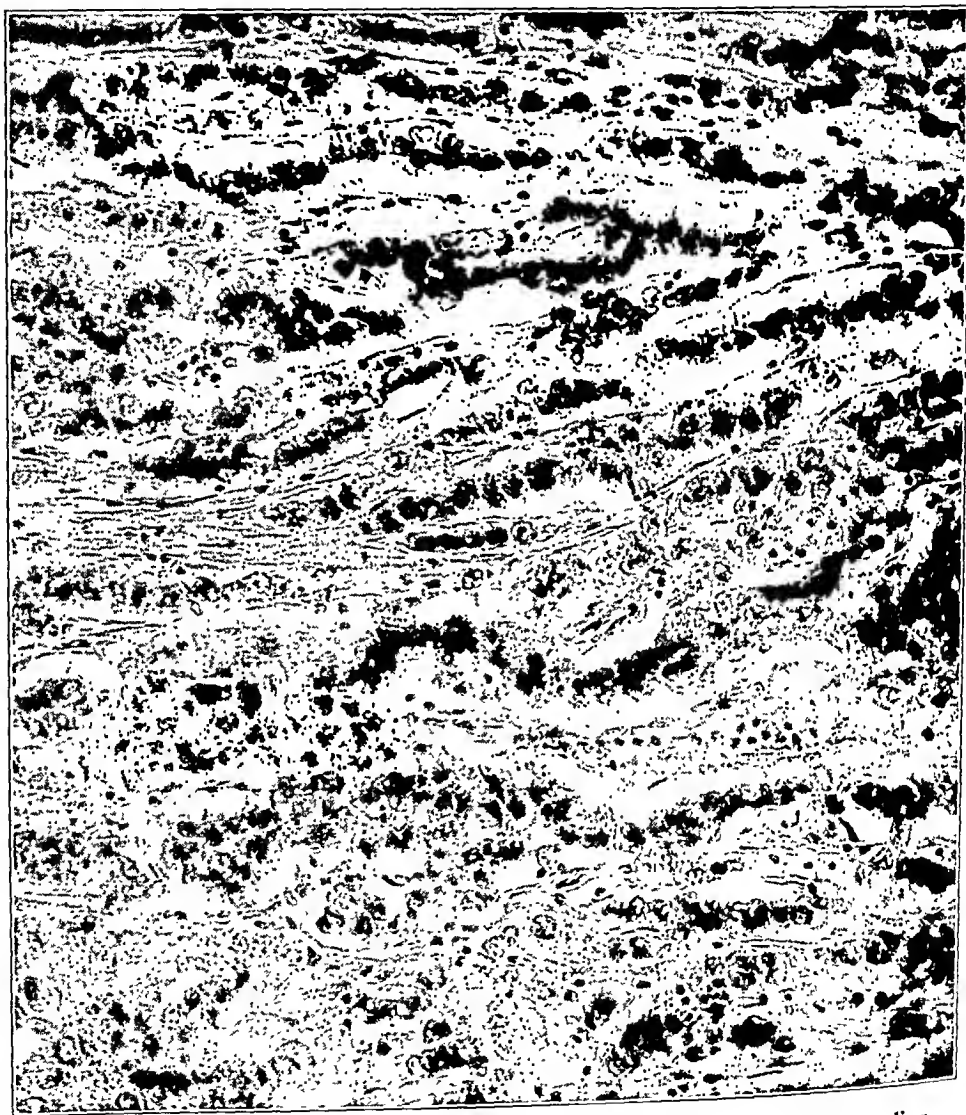


Fig. 6 (case 2).—Photomicrograph of a dysgerminoma which was first diagnosed as carcinoma.

of the abdomen. Physical examination showed a well developed man 6 feet (183 cm.) tall, broad shouldered, with a heavy voice, female distribution of hair, a small penis, an undescended testicle and a hernia in the left side of the scrotum. The patient was married; his marital relations were normal, but his wife had never become pregnant. An operation revealed undescended testicles with a tumor of the right testicle, fallopian tubes and a uterus but no ovarian tissue. The

tumor, both testicles, the tubes and the uterus were removed. The patient left the hospital in good condition but never regained his health completely. He returned to the hospital six months later with identical complaints. Physical examination at this time revealed a firm, freely movable, tender mass in the right renal region. After cystoscopic examination a right posterior lumbar incision was made, and the kidney was exposed; it was found to be embedded in a large mass of tumor tissue, and radon seeds were implanted. Seven emanation seeds containing 3 milli-

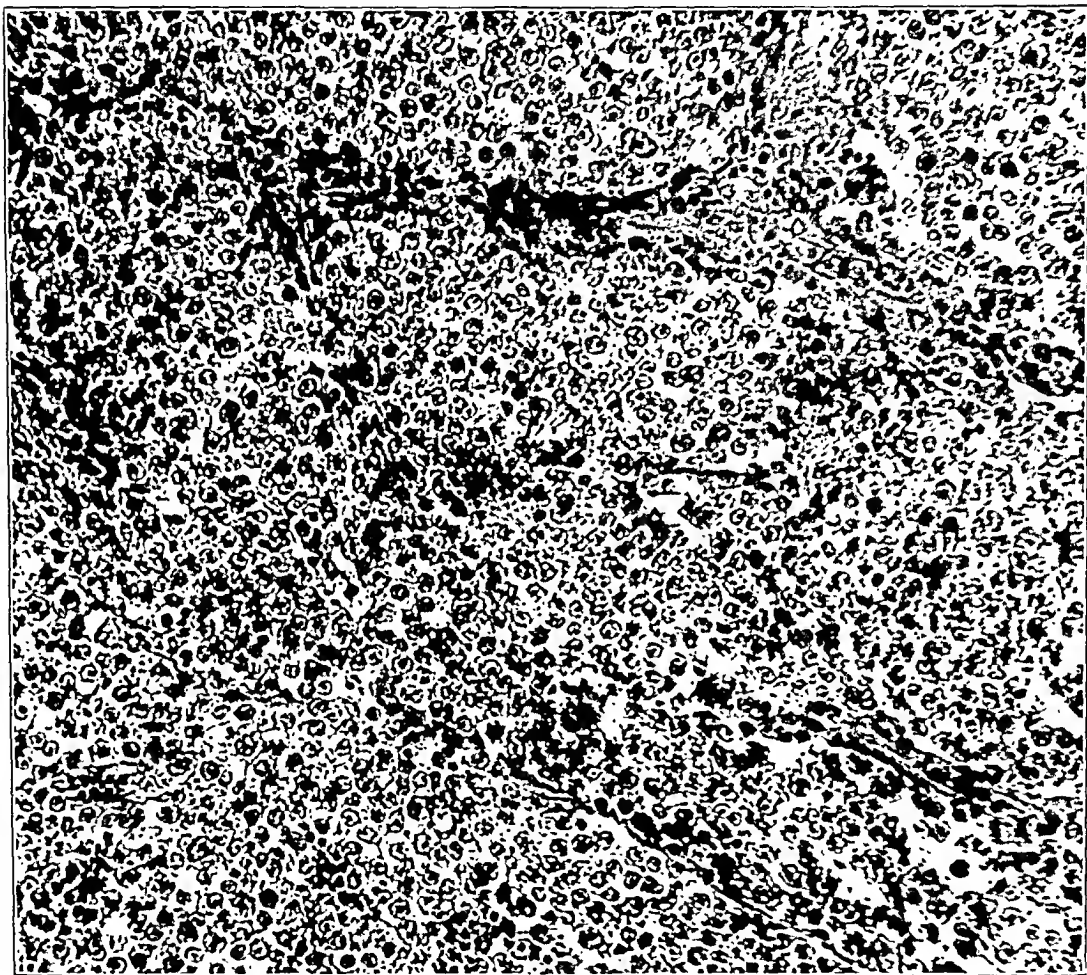


Fig. 7 (case 3).—Photomicrograph of a dysgerminoma which occurred in a unipara aged 26.

curies each were implanted, making a total dose of 2,771 milligram hours. Two months later this dose was repeated. The microscopic diagnosis was dysgerminoma (fig. 9). Five years after the original operation (Feb. 22, 1937) the patient was well, weighing 230 pounds (104 Kg.) and doing manual labor. This case illustrates the more advanced age at which the tumors occur in men and in pseudo-hermaphrodites. This is the second case with widespread recurrence in the lymph nodes in which the condition responded to irradiation.

CASE 6 (Dr. V. Norwood, Baltimore).—P. P., a woman aged 26, married, complained of dizziness, nausea and a heavy feeling in the head for three weeks. The menstrual periods began at the age of 14; they were regular, of three days' duration and accompanied by profuse bleeding and by dysmenorrhea. There was no record as to whether the patient had ever been pregnant. Physical examination revealed a well developed, well nourished woman. Routine pelvic examination showed a small tumor of the left ovary. At a second examination, six months later, it was noted that the tumor had increased threefold, and operation

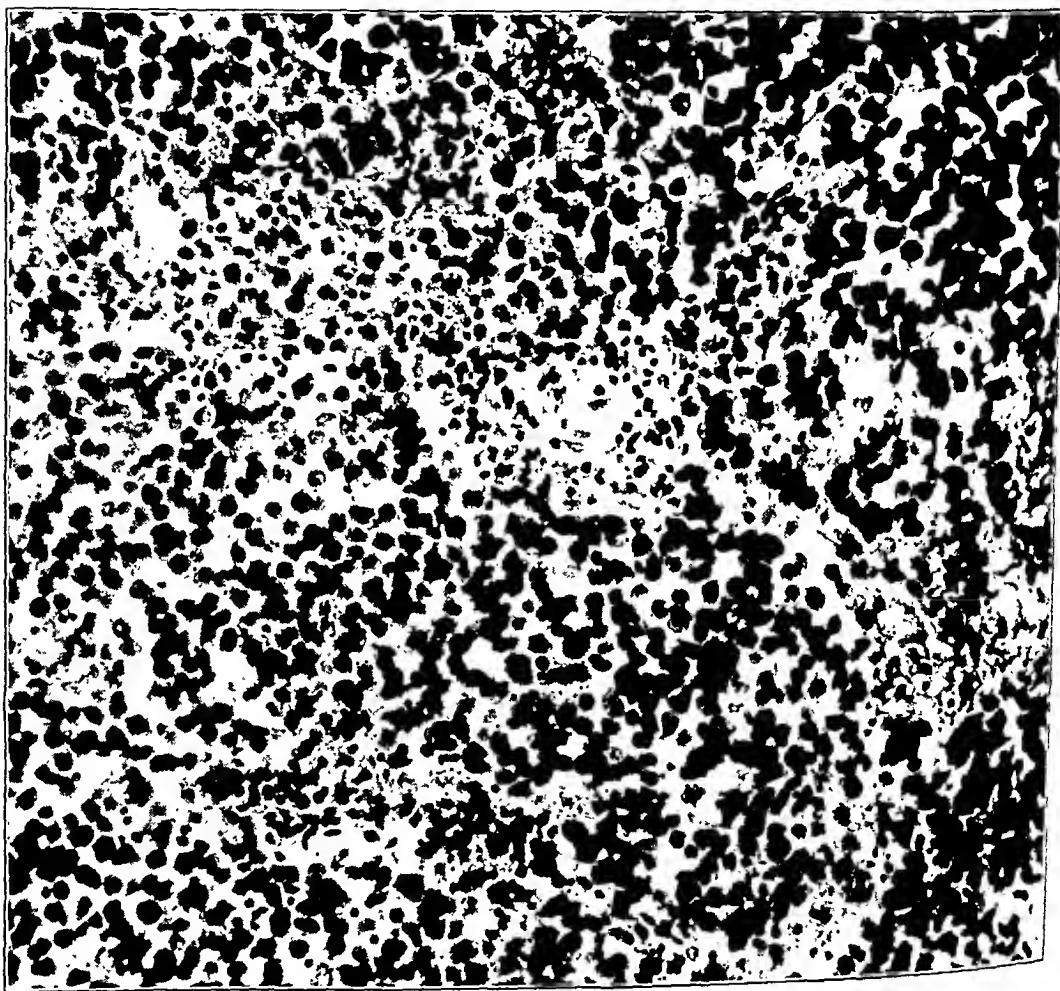


Fig. 8 (case 4).—Photomicrograph of a dysgerminoma which occurred in a girl aged 13. The lesion was bilateral.

was advised. At operation a large, freely movable mass was found occupying the region of the left ovary, and a mass the size of an orange was observed in the left tube. The right ovary was normal. A salpingo-oophorectomy was performed on the left side, and the patient was well six years later (1930) with no evidence of recurrence. Microscopic examination of the tumor showed a typical dysgerminoma. It is of interest to note that this tumor was practically asymptomatic.

CASE 7 (Dr. Louisa Keasbey, Lancaster, Pa.).—A woman aged 38 had normal menstrual periods and had had ten normal pregnancies. In a routine pelvic examination at the time of a thyroidectomy a mass was discovered, which grew rapidly for six months; at the end of this time an operation was advised. Exploratory laparotomy was performed, and a solid circumscribed tumor of the ovary was excised; the tumor weighed 2,340 Gm. After the operation the patient was given massive doses of roentgen therapy. The microscopic diagnosis was dysgerminoma. Two years after the abdominal operation she was reported well.

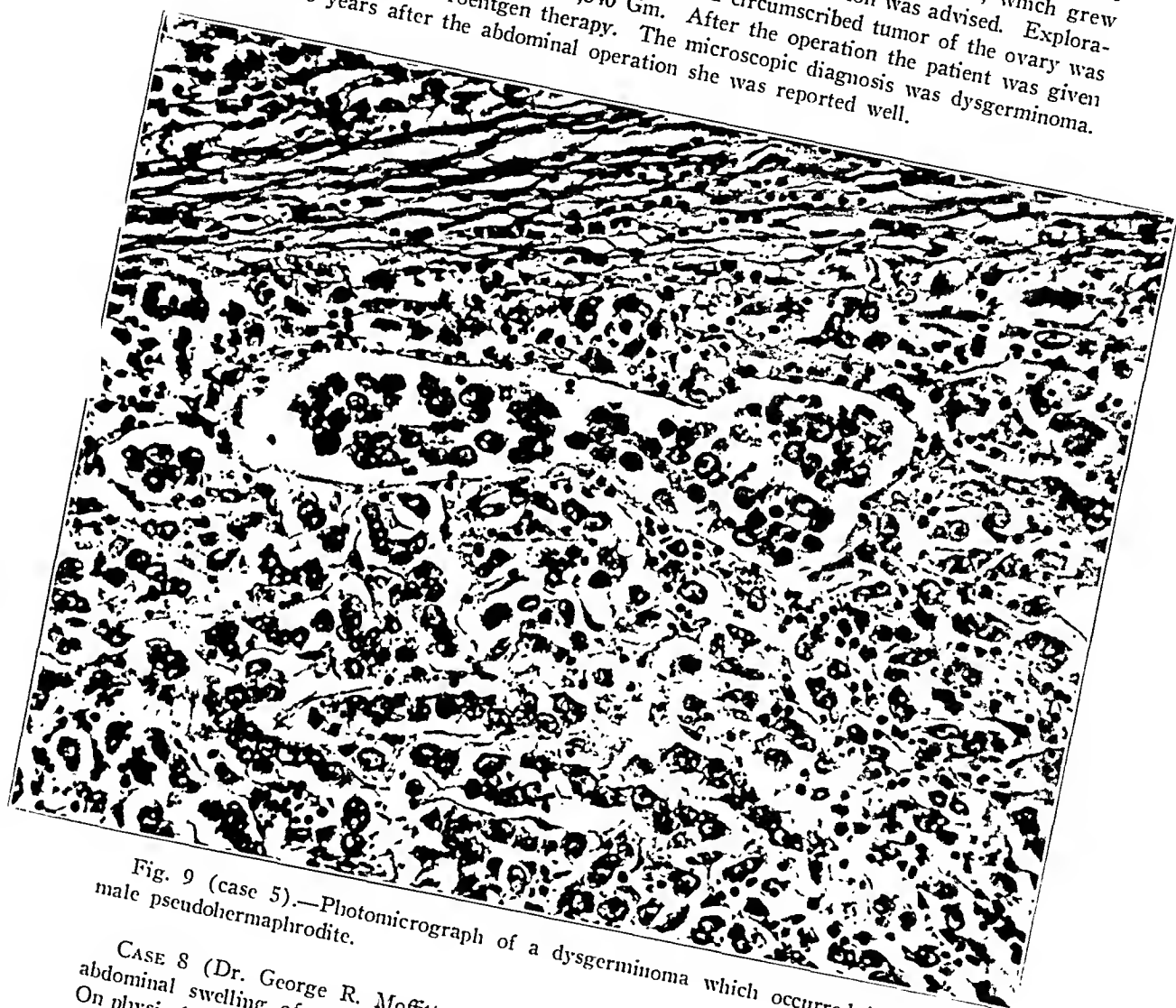


Fig. 9 (case 5).—Photomicrograph of a dysgerminoma which occurred in a male pseudohermaphrodite.

CASE 8 (Dr. George R. Moffitt, Harrisburg, Pa.).—A girl aged 12 had an abdominal swelling of six months' duration. No menstrual history was given. On physical examination the child appeared emaciated. The ankles were edematous, and there was abdominal swelling with signs of intra-abdominal fluid. No tumor was palpable. A laparotomy was performed, and a large tumor arising from the right ovary was removed. There was marked ascites. The child was reported well four months after the operation. Although ascites is generally considered a bad prognostic sign, in this case the tumor was well circumscribed and easily removed. The histologic character of this tumor is shown in figure 10.

CASE 9 (Dr. E. D. Funk, Reading, Pa.).—L. B., a woman aged 18, began to menstruate at the age of 12. The periods were regular; there was a moderate amount of dysmenorrhea. She had noticed a painless progressive swelling of the abdomen for the past six months. A constant, sticking pain in the right side had been present for one week. Physical examination showed a distended abdomen and a mass extending from the pelvis to the umbilicus. The mass was hard, nodular, slightly movable and dull to percussion; no evidence of fluid was observed. There was also some tenderness in the right flank. The external genitalia were

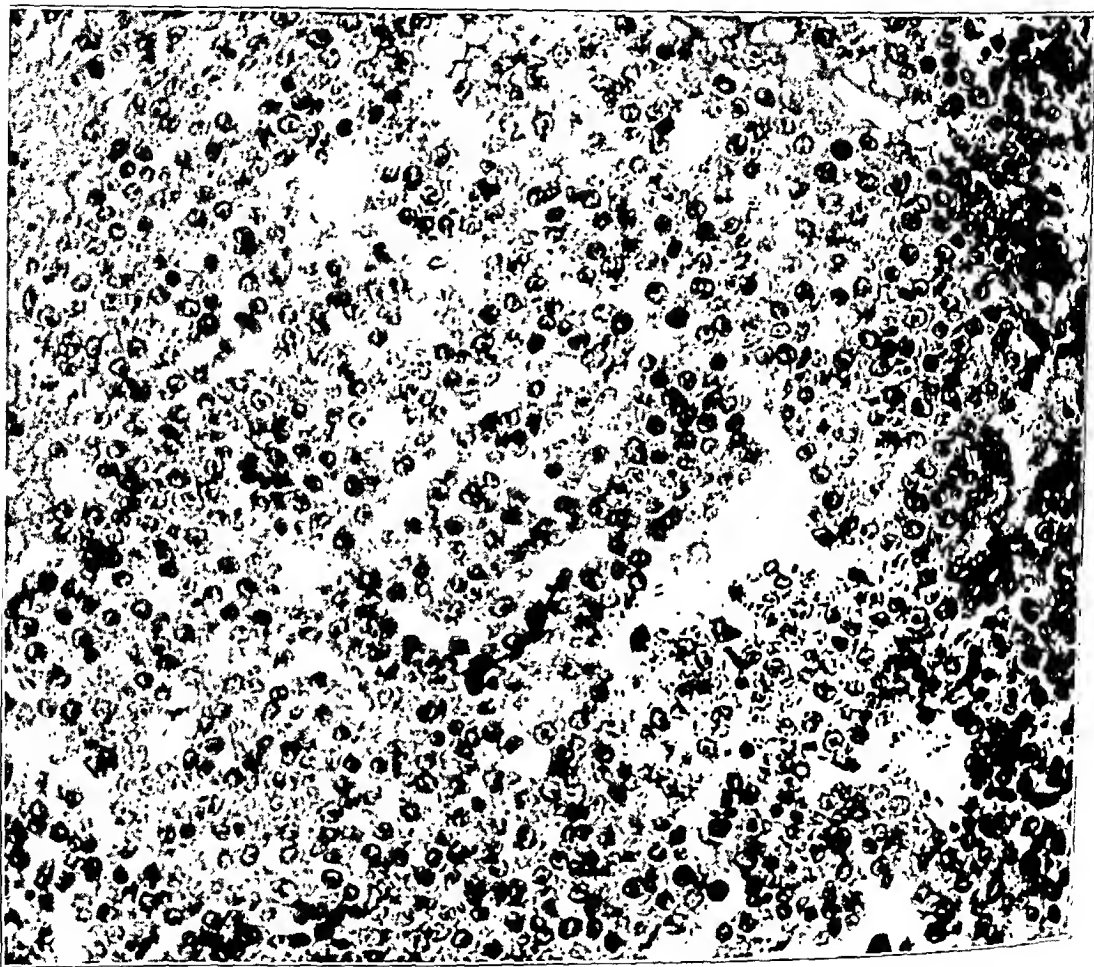


Fig. 10 (case 8).—Photomicrograph of an ovarian tumor which occurred in a girl aged 12.

normal. An exploratory laparotomy revealed a tumor of the right ovary, measuring 4 by 13 by 11.5 cm. and weighing 2,010 Gm. A salpingo-oophorectomy on the right side was performed. The gross specimen was smooth, bosselated and pinkish white. The cut surface was smooth, firm and grayish. There were no cystic or hemorrhagic areas. The microscopic diagnosis was dysgerminoma of the right ovary. Four months after the operation the patient was reported well with no evidence of recurrence (January 1937).

CASE 10 (Dr. G. W. Ramsay, Washington, Pa.).—A woman aged 28, married, began to menstruate at the age of 14. The menses were scanty and irregular;

six years before the present illness they ceased entirely. There were no pregnancies. For two years the patient had complained of a painless enlargement of the abdomen, which had become more marked two months prior to hospitalization. This was accompanied by pain in the sides and in the back. Examination revealed small but well formed breasts. The external genitalia were normal. An operation was performed, and a well encapsulated tumor of the right ovary was removed. The patient died four days after the operation. On gross examination the tumor was irregular and coarsely nodular. It measured 18 by 15 by 8 cm.

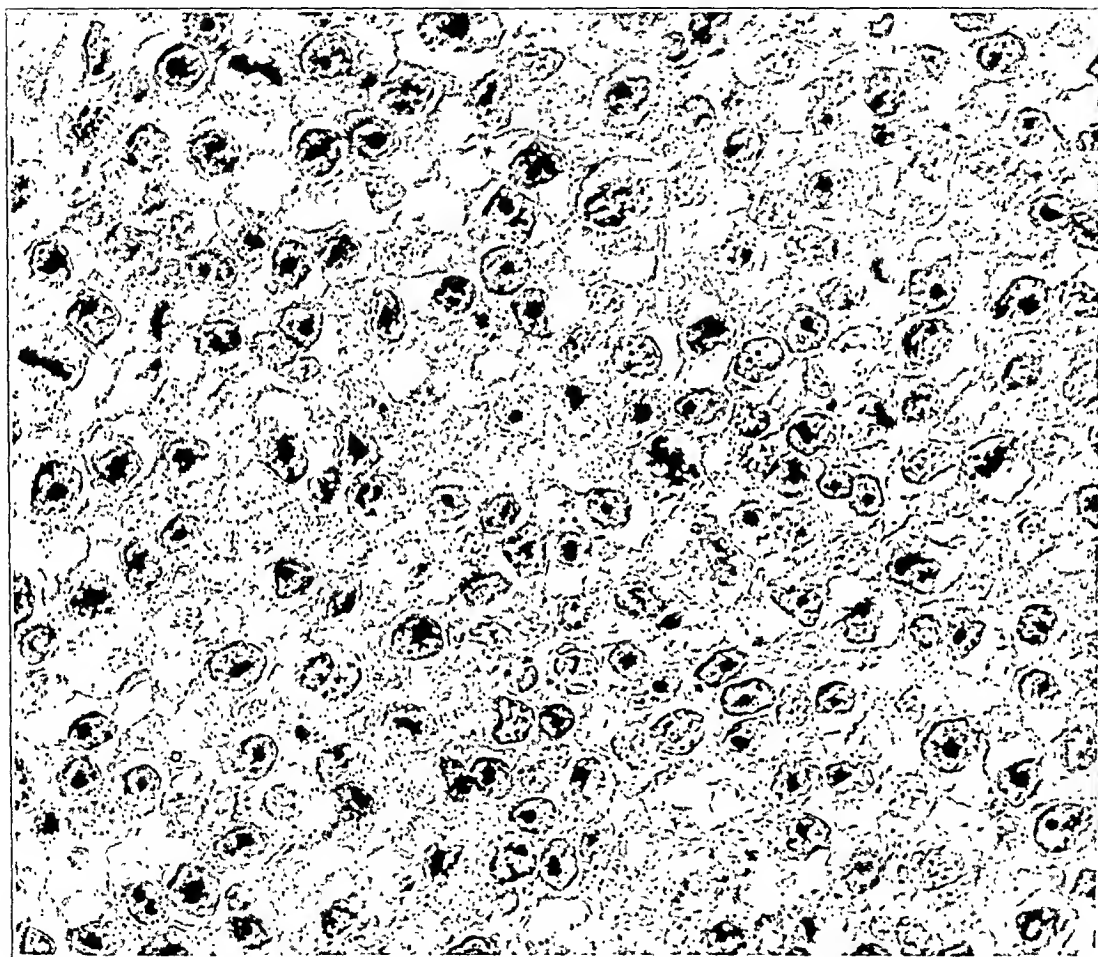


Fig. 11 (case 10).—High power photomicrograph showing the character of the individual dysgerminoma cells. There are frequent mitotic figures. The patient died four days after the operation.

and weighed 1,300 Gm. The cut surface was grayish white and finely granular, with some areas of necrosis. The microscopic diagnosis was dysgerminoma (fig. 11).

CASE 11 (Dr. H. C. Lennon, Philadelphia).—M. D., a white woman aged 22, was first seen because of active pulmonary tuberculosis. The menstrual periods had begun at the age of 14 and had always been regular. She was unmarried and had had no pregnancies.

Soon after coming under observation the patient died of advanced pulmonary tuberculosis. At autopsy the right ovary was found to be symmetrically enlarged, measuring 4.5 cm. in diameter. On section a firm, homogeneous, pale encapsulated mass measuring 3.5 cm. in diameter was found embedded in the central portion of the ovary. On microscopic section this nodule showed the typical picture of dysgerminoma (fig. 12).

Clinically the case is interesting in view of the absence of symptoms and the association with tuberculosis. There are cases reported in the literature in which

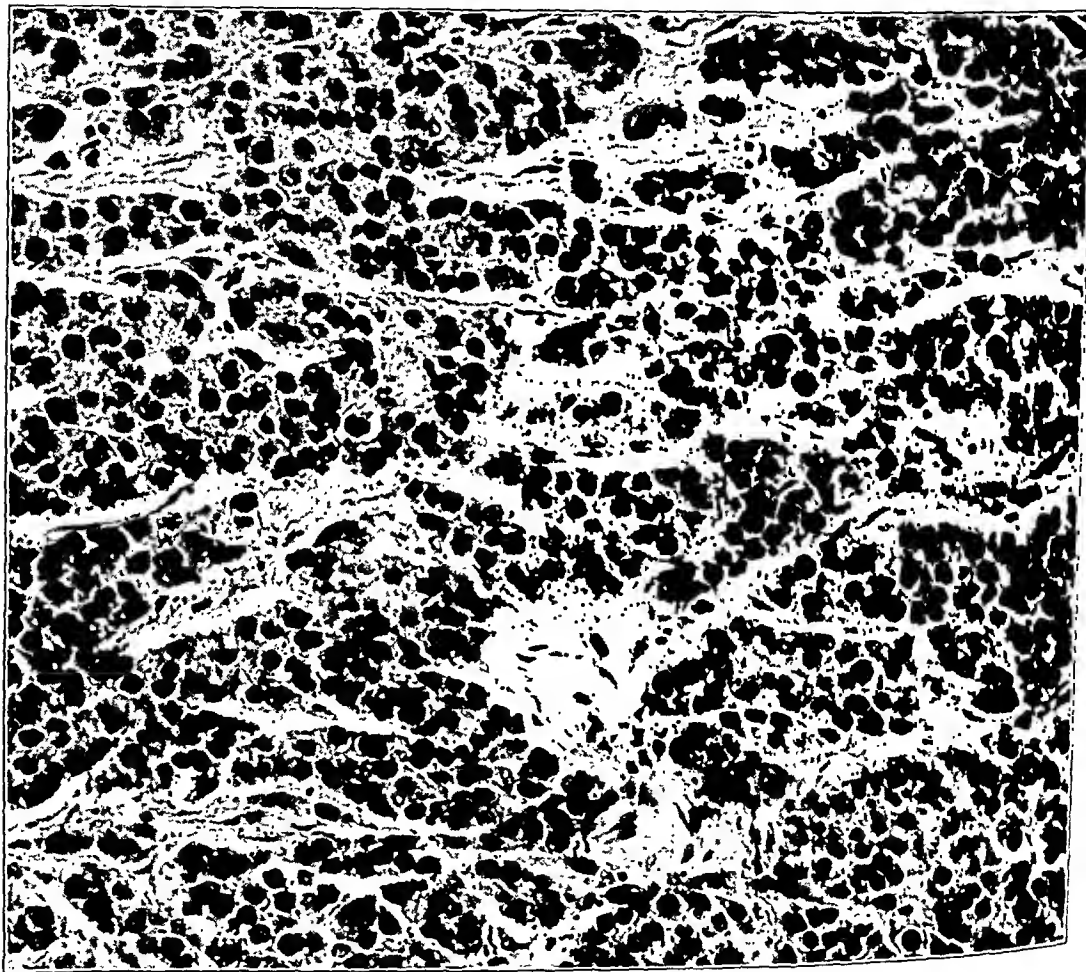


Fig. 12 (case 11).—The photomicrograph of this tumor shows a striking similarity to the medullary cords seen in the developing gonad.

this type of tumor was associated with tuberculosis, and Schiller laid great emphasis on this fact and on the occurrence of giant cells in the tumor.

The small size of the tumor indicates an early lesion. Its location in the hilus of the ovary suggests origin from an embryonal rest, either from the medullary cords or from the indifferent germinal cells of the ovary.

CASE 12 (Dr. E. L. Armstrong, Erie, Pa.).—M. C., a woman aged 30, was admitted to the hospital because of nausea and vomiting associated with tenderness in the lower left quadrant of the abdomen. These symptoms had appeared one

year previously, when the patient fell and injured her left side, and had been gradually increasing in severity. There was loss of weight, anorexia and lassitude.

The patient was found to be a pseudohermaphrodite. There was a heavy beard, requiring daily shaving, and a heavy growth of hair covered the extremities. The voice was deep. The skeletal and muscular development was masculine, and the breasts were flat. Examination of the genitalia revealed excessive pubic hair with feminine distribution, a hypertrophied clitoris and perineal hypospadias with the posterior commissure intact. There was no evidence of labial testes. There was a rudimentary vagina, which admitted one finger, and a small cervix was observed, flush with the vaginal mucosa. On rectal examination a firm mass could be felt occupying the left adnexal region and extending into the abdomen.

At operation a spherical tumor 4 cm. in diameter was found lying in the left broad ligament, adherent to the sigmoid flexure of the colon and to the rectum. The tumor was shelled out easily by blunt dissection; there was no pedicle and no attachment to the ovaries, both of which were present. The uterus was infantile. The microscopic diagnosis was dysgerminoma (fig. 13).

The patient was discharged in good condition. However, she was readmitted four months later, with a recurrence of the nausea, vomiting and abdominal discomfort. Examination at this time revealed a small, firm mass in the left lower quadrant of the abdomen, suggesting a recurrence of the tumor. It was also noted at this examination that she had lost the male secondary sexual characteristics to a great extent. As the patient refused to undergo a second operation she was given roentgen therapy. The result was regression of the abdominal mass and complete alleviation of the symptoms.

Three years later she was admitted to the hospital again, this time with lobar pneumonia of the right lung which proved fatal in six days. On this admission it was stated that she had been well during the three year interval, and on physical examination the female sexual characteristics predominated. There was no evidence of a recurrence of the abdominal growth.

In this case there was regression of the male sexual characteristics in a pseudohermaphrodite following extirpation of a dysgerminoma. Such an occurrence has never been reported in the literature to my knowledge, and in view of my conception of the dysgerminoma as a nonsecretory tumor, it would seem that the phenomena in this case were due to coincidence rather than an effect of the tumor.

Here again there was apparently a remarkable response of the recurring tumor to roentgen therapy.

CASE 13 (Dr. J. J. Shank, Waynesboro, Pa.).—O. S., a girl aged 12, entered the hospital complaining of progressive enlargement of the abdomen. On physical examination a large mass was palpable, filling the entire right lower quadrant of the abdomen and extending into the right upper quadrant. A tentative diagnosis of renal tumor was made preoperatively. At operation a large pedunculated tumor was found arising in the right broad ligament. It completely filled the pelvis, and the upper pole was free in the abdominal cavity. There were extensive adhesions to the peritoneum, the colon, the omentum and the small intestine. The tumor and the appendix were removed.

The tumor weighed 1,293 Gm. and was surrounded by a dense fibrous capsule. Microscopically the tumor showed the characteristics of a dysgerminoma.

The patient was discharged in good condition, and when last heard from, seven and one-half years after the operation, she was in excellent health, with no evidence of recurrence or metastases.

CASE 14 (Dr. Herman H. Van Horn, Harrisburg, Pa.).—M. S., a girl aged 13, entered the hospital complaining of pain in the right lower quadrant of the abdomen and also of nausea and vomiting of three days' duration. She had had recurrent

attacks of pain in the lower part of the abdomen since the age of 6 years. Physical examination revealed a mass the size of a grapefruit in the midline, arising in the pelvis and extending almost to the umbilicus. This mass was dull to percussion, freely movable and not apparently tender. At operation a solid tumor was found, arising in the right broad ligament and replacing the right ovary. The tumor and the right fallopian tube were removed, together with the appendix. The tumor measured 14 by 9 by 9 cm. and weighed 500 Gm. It was completely encapsulated and solid except for one small central cavity containing blood. Micro-

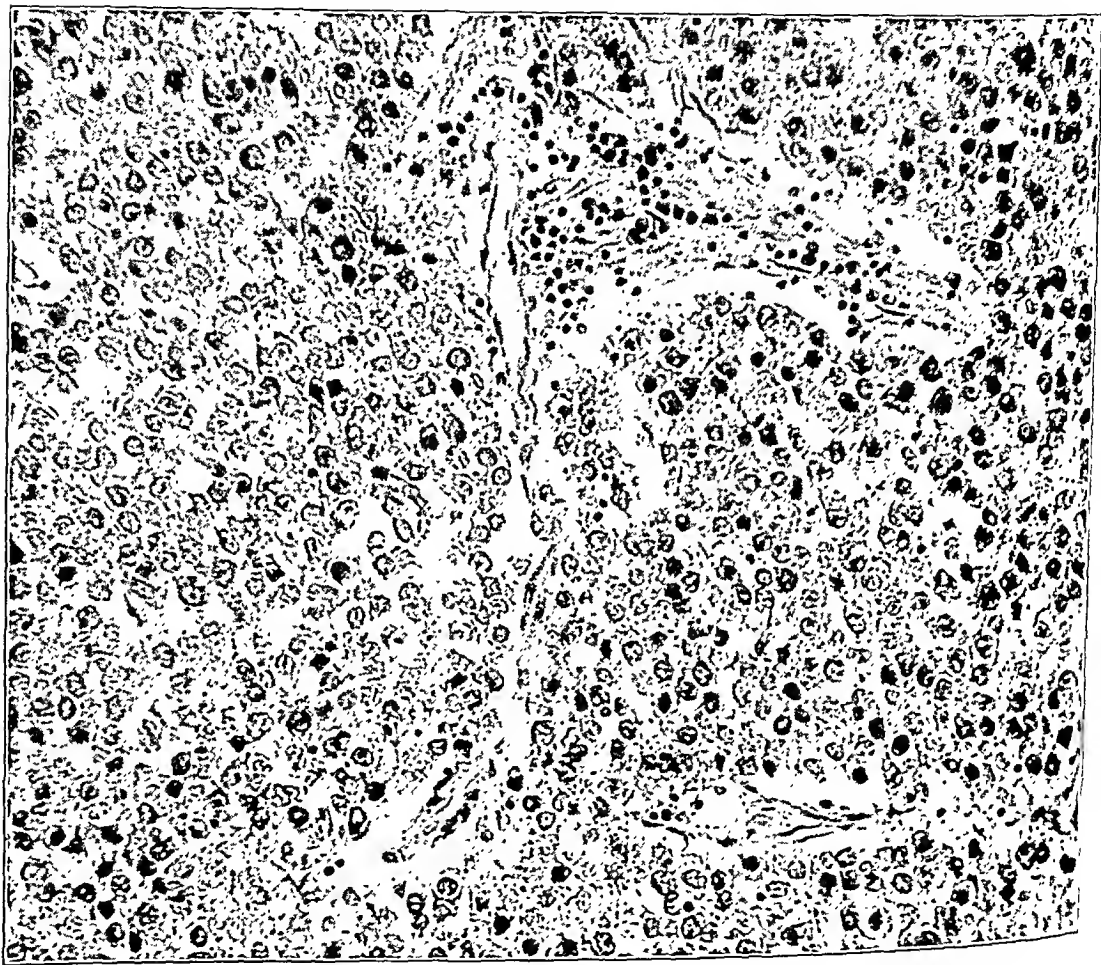


Fig. 13 (case 12).—Photomicrograph of a dysgerminoma which occurred in a female pseudohermaphrodite.

scopic examination revealed a dysgerminoma. The patient was reported well with no evidence of recurrence or metastasis two years and ten months after the operation. The menstrual periods were normal.

CASE 15 (Dr. Helen Ingleby, Philadelphia).—A woman aged 34 noticed increasing abdominal enlargement during a period of six months. The menstrual history was entirely normal. She had had one full term spontaneous delivery fourteen years prior to the present illness. At operation she was found to have a tumor of the right ovary, measuring 20 by 16 by 9 cm., with an irregular

nodular surface. On section it was found to be solid throughout; the cut surface was pale and firm and was divided by dense fibrous septums. Microscopic examination showed typical dysgerminoma.

CASE 16 (Dr. Phillip Jaisohn, Media, Pa.).—R. N., a white woman aged 22, was admitted to the hospital complaining of pain in the lower part of the abdomen, present for one week and of an abdominal mass which she had first noticed six months previously. At operation a tumor was found arising from the left ovary. This tumor was encapsulated. It measured 13 by 9 by 5 cm. The smooth, white glistening surface was continuous with the serosa of the ovary, which was located on the anterior superior aspect of the tumor mass. The ovary was somewhat enlarged and contained a serous cyst. The cut surface of the tumor showed it to be compact, with dense areas of stroma. On microscopic examination the tumor proved to be a dysgerminoma.

CASE 17 (Dr. Oliver Lohr, New York).—A white woman aged 31 came to the hospital complaining of a hard mass in the abdomen. No accurate menstrual or obstetric history was available. Physical examination revealed a well developed normal woman with no evidence of pseudohermaphroditism. On abdominal examination multiple hard, nodular masses could be felt in both lower quadrants of the abdomen. On pelvic examination the uterus was found to be irregularly enlarged, and firm, nodular masses were palpated in both adnexal regions. The Asehlheim-Zondek test gave a negative reaction.

At operation tumors were found replacing both ovaries and involving the retroperitoneal glands. The uterus was also invaded by the tumor tissue and contained, in addition, a small fibroid. The patient survived the operation but died within the month. Autopsy confirmed the operative findings.

The pathologic diagnosis was bilateral dysgerminoma of the ovaries with invasion of the pelvis and uterus.

CASE 18 (Dr. F. P. McNamara, Dubuque, Iowa).—A girl aged 14 consulted a physician because of abdominal swelling and cramplike pain in the region of the umbilicus. The menses had been regular and normal. Four months prior to the onset of the present illness she had begun to have severe dysmenorrhea, necessitating two days' rest in bed during each period. There had been loss of weight.

Physical examination revealed a normally developed girl with an abdominal mass arising in the pelvis and reaching 3 fingerbreadths above the umbilicus; it was approximately 20 cm. in diameter, nodular, hard and slightly movable. Rectal examination showed this mass to arise apparently from the left ovary. It completely filled the pelvis. Neither the liver nor the spleen was palpable. A tentative diagnosis of ovarian tumor was made.

At operation a large, solid nodular tumor of the left ovary was found. The right ovary was cystic, and the spleen, the pancreas and the left kidney were enlarged and nodular. The ovarian mass only was removed. The pathologic diagnosis was dysgerminoma of the left ovary with generalized visceral metastases.

The immediate postoperative course was uneventful. The patient was next seen two years later; there were nodular masses throughout the abdomen. She was extremely cachectic. Roentgen therapy was instituted, and the tumor masses promptly receded. She gained weight, lost her haggard appearance and for a year and a half seemed almost like a normal girl of 16. The neoplasm then reappeared, and this time it did not respond to roentgen therapy. She failed rapidly and died four years after the onset of the first symptoms.

CASE 19 (Dr. Vernon Norwood, Baltimore).—A woman aged 28 was admitted to the hospital after an attack of pain in the lower part of the abdomen and nausea of twenty-four hours' duration. The menstrual periods had been regular.

Examination revealed a protuberant abdomen with a firm mass on the right side, extending from the pelvis to the umbilicus. The clinical impression was right ovarian cyst with torsion of the pedicle. Laparotomy was performed. A tumor the size of a man's head was found in the region of the right ovary. The peritoneal cavity was studded with metastases, and a secondary growth the size of an adult fist was found in the omentum. The ovarian tumor only was removed. Ascites developed after the operation, and the patient died one month after removal of the ovarian tumor. A description of the pathologic specimen is not available.

The sections of the tumor were unusual (fig. 3). They showed typical dysgerminoma tissue associated with a vascular malignant growth containing many large spindle cells and epithelial cells, suggesting chorionic tissue. A few giant cells were scattered through this vascular tissue. The microscopic diagnosis was dysgerminoma associated with atypical chorionic tissue or sarcoma of the ovarian stroma.

SUMMARY

The data on 79 cases of dysgerminoma reviewed in the literature are summarized, together with those on a series of 19 cases recorded in the laboratory of surgical pathology. Dysgerminoma is a relatively rare tumor, the incidence being under 3 per cent of all malignant ovarian neoplasms. It occurs in young persons, usually in those under 30 years of age, 48 per cent of the growths being in the right ovary and 26 per cent bilateral. Occasionally the tumor is associated with sexual underdevelopment or maldevelopment. Rapid growth of the neoplasm results in an abdominal mass which on pelvic examination is found to be an elastic, nodular tumor arising from the adnexal region; in the benign form it is well circumscribed and freely movable; in the more malignant types, infiltrative, with extensive metastatic involvement of the retroperitoneal glands, the peritoneum, the omentum, the bladder and the rectum. Metastases to distant organs are extremely rare, and metastasis to the lungs has not been reported. Microscopically, dysgerminoma is characterized by large, discrete germinal cells of a caviar-like appearance and by abundant lymphoid stroma. Dysgerminoma may be associated with other forms of ovarian tumor, such as teratoma or chorioepithelioma. I have found it impossible to differentiate the benign and the malignant form histologically. However, from the history and the findings at operation it is sometimes possible to prognosticate correctly. These tumors have a mortality between 35 and 60 per cent, with a slightly higher rate of recurrence and metastasis. These figures are based on follow-up reports found in a series of 50 cases reported in the literature and on the results of treatment in 17 of 19 cases followed in the present series. The treatment of choice is removal of the tumor and the affected tube and ovary only. Recurrences and metastases are best treated by excision and roentgen therapy, although in 1 case the tumor was successfully treated by roentgen therapy alone. In cases in which removal of the mass is impossible the patients should be given the benefit of irradiation therapy.

BIBLIOGRAPHY

- Babes, A.: Arch. f. Gynäk. **135**:545, 1929.
- Bonnet, P.: Lyon chir. **25**:191, 1928.
- Chenot, M.: Contribution à l'étude des épithéliomes primitifs de l'ovaire, Thesis, Paris, no. 129, 1911.
- Chevassu, M.: Rev. de chir., Paris **30**:628, 1910; Tumeurs du testicule, Thesis, Paris, no. 193, Paris, G. Steinheil, 1906.
- Desmarest and Masson: Bull. et mém. Soc. anat. de Paris **87**:448, 1912.
- Döderlein, G.: Zentralbl. f. Gynäk. **60**:1027, 1936.
- Du Pont, R., and Simard, L. C.: Bull. et mém. Soc. anat. de Paris **95**:124, 1925; Bull. Soc. d'obst. et de gynéc. **14**:195, 1925.
- Dworzak, H.: Arch. f. Gynäk. **151**:281, 1932.
- Fauvet, E.: Zentralbl. f. Gynäk. **58**:2162, 1934; **60**:675, 1936.
- Ferguson, R. S.: Am. J. Cancer **18**:269, 1933.
- Frankl, O.: Zentralbl. f. Gynäk. **60**:1682, 1936.
- Gilliard, A.: Strahlentherapie **52**:226, 1935.
- Gross, cited by Matsner.
- Hajek, O.: Zentralbl. f. Gynäk. **59**:317, 1935.
- Hammant, A., and Cornil, L.: Bull. Soc. d'obst. et de gynéc. **14**:606, 1925.
- Hartmann; Ménétrier, P., and Isch-Wall, P.: Bull. Assoc. franç. p. l'étude du cancer **11**:319, 1922.
- Hoch, J.: Bull. Assoc. franç. p. l'étude du cancer **19**:476, 1930.
- Keller, cited by Matsner.
- Klaften, E.: Zentralbl. f. Gynäk. **57**:36, 1933; Arch. f. Gynäk. **158**:544, 1934.
- Klein, H. O.: Arch. f. Gynäk. **158**:9, 1934.
- Laffont and Bonafos: Bull. Soc. d'obst. et de gynéc. **23**:642, 1934.
- Lubarsh, cited by Matsner.
- Matsner, E. M.: Arch. f. Gynäk. **119**:563, 1923.
- Ménétrier, P.; Pcyron, A.; Isch-Wall, P., and Lory: Bull. Assoc. franç. p. l'étude du cancer **11**:185, 1922.
- Meyer, R.: Arch. f. Gynäk. **109**:212, 1918; **123**:675, 1925; **145**:2, 1931; Zentralbl. f. Gynäk. **49**:1244, 1925; Am. J. Obst. & Gynec. **22**:697, 1931.
- Neumann, H. O.: Ztschr. f. Geburtsh. u. Gynäk. **98**:78, 1930; Arch. f. Gynäk. **130**:742, 1927; **131**:477, 1927.
- Pick, cited by Matsner.
- Reifferscheid, W.: Ztschr. f. Geburtsh. u. Gynäk. **110**:273, 1935.
- Rössle: Monatschr. f. Geburtsh. u. Gynäk. **35**:244, 1912.
- Schiller, W.: Arch. f. Gynäk. **158**:1, 76 and 89, 1934; J. Obst. & Gynaec. Brit. Emp. **43**:1134, 1936.
- Szathmáry, Z.: Arch. f. Gynäk. **153**:333, 1933.
- Tietze, K.: Arch. f. Gynäk. **146**:197, 1931.
- Wallis, O.: Zentralbl. f. Gynäk. **57**:729, 1933.
- Wolfe, S. A., and Kaminester, S.: Am. J. Obst. & Gynec. **29**:71, 1935.
- Zacharias, cited by Matsner.
- Zimmerman, cited by Matsner.
- Zondek, B.: Gonadotropic Hormone in Diagnosis of Chorionepithelioma, J. A. M. A. **108**:607 (Feb. 20) 1937.
- Zucker, cited by Matsner.

INFECTIONS OF THE HAND

THREE YEARS' EXPERIENCE IN A CLINIC FOR STUDY OF WHITLOW

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A clinic for the study of whitlow was started at University College Hospital at the end of 1933. The patients seen at the clinic, which is held once a week, are referred from the casualty department because of minor injury of the hand and whitlow, the latter being defined as a focal infection of the hand. The function of the clinic is advisory, treatment remaining in the hands of the casualty officers.

INCIDENCE

In the three years from 1934 to 1936, inclusive, 41,474 patients were seen in the surgical division of the casualty department. Of this number, 388 patients had infection or injury of the hand, that is, such patients account for just under 1 per cent of the patients in the surgical division of the casualty department (table 1). The slight rise in the incidence of such disorders in 1936 is probably due to the greater care now taken to refer the patients to the clinic. The figures given in table 1, showing the number of cases of injury and infection observed

TABLE 1.—*Incidence Among Patients in the Casualty Surgical Department*

Year	No. of Patients	Whitlows and Injuries	Percentage
1934.....	13,312	118	0.88
1935.....	13,344	119	0.89
1936.....	14,818	151	1.02
Total.....	41,474	388	0.93

at the clinic, do not include all such cases in which treatment was given at the hospital during this period, for the following reasons:

1. After the clinic was started, some time passed before the mechanism of collecting its patients was working efficiently, and some patients missed attendance.

2. Some patients attend for dressings at night, and a few of these are unable to attend the regular sessions of the clinic.

3. Patients with serious symptoms are usually admitted to the wards as soon as they are seen and on discharge may or may not attend the clinic.

From the University College Hospital.

4. Injuries and infections occurring among the members of the nursing staff are not seen at the clinic.

With the exception of the patients among the nursing staff I do not think that many patients have missed attendance at the clinic.

AGE

As may be seen in table 2, in about 60 per cent of cases the injury or infection occurred in the second or the third decade of life, and cases were more or less equally distributed between them.

TABLE 2.—*Distribution According to Age*

Age (Years)	Number of Patients
0-10.....	24
11-20.....	128
21-30.....	104
31-40.....	51
41-50.....	50
51-60.....	21
Over 60.....	10
Total.....	388

Youngest 1 year; oldest 75 years.

OCCUPATION

There was a great variety of occupations. Children, including school children, accounted for 18 per cent of the patients, and the majority of the remainder were manual laborers, craftsmen, housewives and domestic servants. There were comparatively few clerical workers.

SEX

The number of male and of female patients affected by casualties is approximately equal, and this was true of the series presented, 195 patients being men and 193 women. Injury occurred nearly twice as frequently in men as in women, and paronychia, nearly twice as frequently in women as in men. In the former class the distribution is probably due to the nature of the occupation pursued; in the latter, to the practice of manicuring the nails. In all 6 cases of carbuncle of the fingers or the hand the patients were men. This incidence may be associated with the greater hairiness of the male hand. For the other types of infection the incidence was about equal in both sexes, or the number of cases recorded was too small to enable the drawing of any conclusions.

TRAUMA

Of the 388 cases 61 were cases of injury. If this number be subtracted, 327 cases of infection remain, and of these there was a history of injury in 192, or 58.7 per cent. Only those cases in which the

patient could describe the type of injury and the time of its infliction are included in the group in which there was a history of injury, although in many other cases it seemed probable from the appearance of cuts and scratches on the hands that injury had preceded infection. All patients with a history of trauma were asked whether precautions had been taken to prevent infection. Only 3 had received first aid, although it was available to many more. The injuries were in most cases comparatively trivial; they varied in character, injuries due to crushing, to cuts and to pricks being the commonest. A common complication of trivial injury is the entry of a foreign body. If the injury is followed by infection the retention of the foreign body will delay or prevent healing. In 4 cases in the series, a retained foreign body caused prolonged suppuration, and in all 4 cases rapid healing followed its removal. In only 1 of these cases was the presence of a foreign body suspected by the patient. In any case of unexpected delay in healing the possibility of a retained foreign body must be considered.

If the various types of infection are considered, it is seen that there is no significant difference between them in the proportion of cases in which trauma precedes infection. Thus, of the cases of infection of the digital pulp, of paronychia and of subcutaneous abscess and cellulitis of the fingers, trauma occurred in 64, 50 and 65 per cent, respectively. With the other types of whitlow the figures were not large enough to indicate the significance of trauma.

HAND AFFECTED

The right hand was affected in 192 cases, the left in 159 and both hands in 6; for 31 patients there was no note as to which hand was affected. No note was made of the right-handedness or left-handedness of the patients, so it is impossible to estimate the importance of this factor.

FINGERS AFFECTED

Table 3 shows that the index and the middle finger and the thumb were affected most frequently and to an equal extent. The ring finger was involved half as frequently as was any of the first three digits, and the little finger half as frequently as the ring finger. This was true of the series as a whole. It is also true of the individual types of infection, with the exception of paronychia, when the number of cases is sufficiently large to be useful. In this type of whitlow the index, the middle and the ring finger are affected equally commonly, and the thumb twice as commonly as any one of these digits.

TYPES OF WHITLOW

The categories in which the cases of this series have been placed are mostly self explanatory. In order to remove any ambiguity it may be stated:

1. In all cases in which the condition was classified as injury the patient came to the hospital with an injury to the hand and was treated for it. Cases in which the patient was first seen when infection had followed injury are included under the appropriate type of infection.

TABLE 3.—*Fingers Affected*

Injury	Type	Thumb	Index	Middle	Ring	Little	Not stated	Total	Remarks
(a) By crushing.....		4	12	12	9	2	1	40	2 patients had 2 fingers affected
(b) Other.....		5	9	7	3	3	0	30	2 patients had 2 fingers and 1 had 3 fingers affected
Infection of digital pulp									
(a) Uncomplicated; acute.		12	21	14	3	3	2	55	1 patient had 3 fingers affected
(b) With necrosis of terminal phalanx.....		5	3	3	1	0	0	12	
Paronychia									
(a) Uncomplicated; acute.		33	11	17	13	7	0	81	2 patients had 2 fingers affected
(b) With infection of pulp		3	2	2	1	0	0	8	
(c) Chronic and recurrent		2	1	3	4	1	0	11	
(d) Pus under distal part of nail.....		3	5	1	2	1	1	13	
Subcutaneous abscess and cellulitis.....		20	27	21	8	11	2	89	
Carbuncle.....		1	1	4	0	1	0	7	
Infection of tendon sheath..		0	2	4	2	0	0	8	
Suppurative arthritis.....		2	2	4	0	0	0	8	
Total.....		99	96	92	40	29	6	365	

2. Cases in which the lesion was classified as subcutaneous abscess and cellulitis of the fingers do not include those of infection of the digital pulp.

3. The group labeled "miscellaneous" includes cases of infections which do not fit into any of the other categories and cases of stiff or painful fingers.

DURATION OF DISABLEMENT

By "duration of disablement" is meant in most cases the period after the onset of the injury or whitlow during which the patient was unable to work.

Among the cases of injury of the fingers by crushing were 5 of compound fracture of the terminal phalanx. In 3 of these the diagnosis was correctly made, and an immediate partial amputation of the terminal phalanx with removal of the nail bed and closure of the wound was

performed. The 3 patients were able to return to work in three weeks. In the other 2 cases the diagnosis was not made until the patient was seen at the whitlow clinic. In 1 the wound healed in four weeks; in the other the fracture became infected, sequestration occurred and the patient was disabled for three months.

TABLE 4.—*Type of Lesion and Duration of Disablement*

Injury	Type	Male	Female	Trauma	Total	Duration of Disablement
(a) By crushing.....		20	13	33	33	27 for 1 to 4 weeks 6 for 6 weeks and longer
(b) Other.....		19	9	28	28	1 not known (ceased attendance) 22 for 1 to 4 weeks 5 for longer than 4 weeks
Total injury.....		39	22	61	61	
Infection of pulp						
(a) Uncomplicated.....		27	33	37	60	4 not known (ceased attendance) 48 for 2 to 3 weeks 8 for 4 to 8 weeks
(b) With necrosis of terminal phalanx		5	7	9	12	2 not known (ceased attendance) 2 for 6 weeks 2 for 8 weeks 6 for 12 weeks
Total infection of pulp.....		32	40	46	72	
Paronychia						
(a) Uncomplicated; acute.....		32	32	42	84	6 not known (ceased attendance) 4 for 1 week 62 for 2 to 3 weeks 12 for 4 to 6 weeks
(b) With infection of pulp.....		2	6	6	8	5 for 3 to 5 weeks 3 for longer than 5 weeks
(c) Chronic and recurrent.....		2	7	1	9	From 5 weeks to 6 months
(d) Pus under distal part of nail..		4	9	8	13	12 for 1 to 3 weeks 1 for 5 weeks
Total paronychia.....		40	74	57	114	
Subcutaneous abscess and cellulitis of fingers		54	35	58	89	3 not known (ceased attendance) 4 for 1 week 55 for 2 to 3 weeks 27 for longer than 3 weeks
Carbuncle of fingers or hand.....		6	0	1	6	1 for 2 weeks 5 for 3 to 4 weeks
Palmar and web abscesses.....		13	7	12	20	3 for 1 to 2 weeks 12 for 3 to 4 weeks 2 for 6 weeks 1 for 8 weeks 2 for 11 weeks
Infection of the flexor tendon sheaths		4	4	8	8	1 not known (ceased attendance) 1 for 2 weeks 6 for 8 weeks and longer
Suppurative arthritis.....		6	3	9	9	1 not known (ceased attendance) 1 for 2 weeks 6 for 8 weeks and longer
Miscellaneous.....		1	6	1	7	
Total cases.....		195	193	253	388	

As may be seen in table 4, necrosis of the terminal phalanx complicating infection of the pulp more than doubles the period of disablement and often leaves the patient with some permanent defect; the sensitive pulp of the finger is usually destroyed. In such cases there was always either a long interval between the onset of pain and the

patient's attendance at the hospital (from nine days to four weeks), or there was a history of two or more operations, which suggested that the first operation either was mistimed or was inadequate. One patient had his finger incised three times by his physician and twice at the hospital before the remnants of the phalanx were amputated.

Of the cases of infection of the flexor tendon sheaths, the diagnosis in 1 was doubtful. The patient was treated with rest and hot fomentations, and the condition, which was perhaps cellulitis, subsided without an operation. Of the 6 cases in which operation was performed, the injury was a cut in 3 instances and a penetrating wound in the others. The periods elapsing between the injury and the patient's admission to the hospital were eleven, fourteen, unrecorded, three, five and fourteen days, respectively. In 3 cases the infection was probably primarily in the tendon sheath; in the others infection in the tendon sheath complicated cellulitis of the finger in 2 and an infection of the pulp in the third. In all 6 the diagnosis was confirmed at operation, and in all these the tendon sloughed. In 2 the finger was eventually amputated, and in all 6 there was severe permanent damage to the hand. The periods of disablement in the cases in which the affected finger was amputated were five and one-half and four months. In 3 other cases, eight, ten and twelve weeks elapsed before the wounds were healed. One patient ceased attendance at the end of eight weeks, with an unhealed wound.

In the cases of suppurative arthritis the joints affected were: the interphalangeal joint of the thumb in 2, the distal interphalangeal joint of the finger in 1, the proximal interphalangeal joint of the finger in 5 and the metacarpophalangeal joint of the finger in 1. Table 3 shows that the thumb and the index and the middle finger were the digits affected. There was a history of injury in all, and the arthritis complicated an infection of the pulp in the first 3 mentioned and cellulitis of the finger in the others. In all there was roentgenologic evidence of osteomyelitis of one or both bones forming the joint. In 1 case the finger was amputated, and the period of disablement was three months. Two patients ceased attendance when they still had sequestrums and discharging sinuses. Two patients had periods of disablement of six weeks, but 1 of these, although he was back at work, had a stiff, painful thumb. Two women had periods of disablement of ten weeks. In both the pulp of the finger had been infected, and in both hyperesthesia of the scar appeared, persisting in 1 case for one year and in the other for eight months. In the remaining 2 cases the periods of disablement were eleven and fifteen weeks, and although there was considerable limitation of movement of the affected joints, the function of the hand was good. With the exception of these 2, all the patients were left with some permanent damage to the hand.

TABLE 5.—Cases in Which the Usual Period of Disablement Was Exceeded

Cases	Period of Disablement	Cause or Supposed Cause of Prolongation
Injury by crushing		
Usual period of disablement 1 to 4 weeks		
1 to 3	6 to 7 weeks	Infection of wound
4	10 weeks	Infection of wound complicated by suppurative arthritis of terminal interphalangeal joint
5	13 weeks	Infection of initially unrecognized compound fracture of terminal phalanx, leading to necrosis of phalanx and sequestration
6	2½ years +	Slight initial infection of wound followed by causalgia
Other injury		
Usual period of disablement 1 to 4 weeks		
1	5 weeks	Subcutaneous abscess of palm from which a needle was removed; injury was a lacerated finger, healed in 3 weeks
2	7 weeks	Stiff fingers
3	10 weeks	Infection of wound and necrosis of terminal phalanx
4	10 weeks	Hyperesthesia of scar
5	6 months	Partial dry gangrene developed during treatment for compound fracture of phalanx; refused amputation
Uncomplicated infection of pulp		
Usual period of disablement, 2 to 3 weeks		
1 and 2	4 to 5 weeks	None found
3	5 weeks	Previous infection of pulp in same finger 8 years before; bone in old scar
4 to 6	6 to 7 weeks	Delay in starting treatment; interval of 10 to 18 days between onset of pain and hospital attendance
7	7 weeks	Inadequate or mistimed operation; two operations
8	8 weeks	Inadequate or mistimed operation; three operations; hyperesthesia of scar
Infection of pulp with necrosis of terminal phalanx		
Shortest period of disablement, 6 weeks		
1 to 2	12 weeks	Hyperesthesia of scar
Paronychia, uncomplicated, acute		
Usual period of disablement, 2 to 3 weeks		
1 to 5	4 to 5 weeks	None found
6 and 7	5 and 6 weeks	Delay in starting treatment; interval of 7 and 14 days between onset of pain and hospital attendance
8 to 11	5 to 6 weeks	Inadequate primary operation for removal of nail; second operation
12	6 weeks	Raynaud's disease
Paronychia, complicated by infection of pulp		
Usual period of disablement, 3 to 5 weeks		
1	6 weeks	Delay in starting treatment; interval of 7 days between onset of pain and hospital attendance
2	10 weeks	Inadequate or mistimed operation; four operations
3	11 weeks	Patient stopped attendance for 4 weeks and on return had necrosis of terminal phalanx
Pus under distal part of nail		
Usual period of disablement, 1 to 3 weeks		
1	5 weeks	Splinter buried in nail bed, overlooked at first operation
Cellulitis and subcutaneous abscess of fingers		
Usual period of disablement, 2 to 3 weeks		
1 to 13	4 to 6 weeks	None found
14 to 20	4 to 6 weeks	Inadequate or mistimed operation; two or more operations
21 to 23	4 to 6 weeks	Delay in starting treatment; interval of 7 to 10 days between onset of pain and hospital attendance
24	3 months	Inadequate or mistimed operation; two operations
25	3 months	Stiff finger
26	3 months	Initial lymphangitis; appearance of residual brachial abscess 2 weeks after cellulitis of finger had subsided
27	4½ months	Gangrene of finger with severe infection of hand; cause unknown
Pain and web abscess		
Usual period of disablement, 3 to 4 weeks		
1 and 2	6 weeks	Both deep abscess of palm; for 1, two operations
3	8 weeks	Deep abscess of palm; initial incision wrongly made on dorsum
4	11 weeks	Web abscess with splinter in hand, stated to have been removed, but finally discharged spontaneously
5	11 weeks	Hyperesthesia of scar
Suppurative arthritis		
Shortest period of disablement, 6 weeks		
1	8 months }	Apparently permanent hyperesthesia of the scar in both cases
2	1 year }	

Of the patients with miscellaneous lesions 1 was a woman aged 20 who had had a chronic ulcer on the dorsum of the ring finger for four weeks when she was first seen. She was treated for another four weeks without improvement, after which, on curettage, a splinter was found, and two weeks later the ulcer had healed.

Table 5 shows the cases in which the usual period of disablement was exceeded; the cause, or supposed cause, of this is indicated. In cases of injury, infection of the wound, and in cases of whitlow, delay in starting treatment, mistimed or inadequate operation and hyperesthesia of the scar were most commonly responsible for this prolongation.

COMMENT

The well known association of trivial injury with infection of the hand is illustrated by the figures given in an early part of this paper. It is likely that if such injury were to receive prompt treatment the incidence of whitlow would be much reduced. This supposition has been confirmed within my own knowledge by the experience of a large engineering firm, which found that the strict application of prophylactic measures to trivial cuts and scratches was followed by a material reduction in the incidence of infection. Such measures are immediate cleansing of the wound, its protection against contamination and a warning to the patient to report immediately if the lesion becomes painful.

With regard to acute infection, certain tendencies in treatment seem to be emerging from physicians' experience, though they cannot yet be looked on as established. They may be stated thus:

1. Operative treatment, short of total extirpation of the affected area, cannot benefit a patient with an acute infection during the period of spread. There is no clear evidence that the supposed "relief of tension" effected by a premature incision ever checks the progress of an infection, whereas such incision almost always precipitates sloughing and actually increases the amount of damage.

2. The function of operation is the evacuation of pus, and it is as important to avoid undue haste in operating as to avoid undue delay.

3. In the early stages treatment must be directed to helping the tissues in their struggle with the infection. The most important elements in this are elevation and absolute immobilization of the limb.

4. While rest is of the greatest value during the stage of acute invasion, it must be discontinued as soon as healing has begun. Disuse of a finger itself may produce serious disablement.

At present too much stress is perhaps laid on the anatomic basis of the treatment of these conditions. Attention is so much focused on the site of the incision and the necessity for early operation "to relieve

tension" that unnecessary operations are apt to be encouraged. It is necessary to state emphatically that premature incision for spreading cellulitis is by no means a harmless blunder; it may determine the onset of sloughing. The plea for early incision is usually stressed in cases of infection of the digital pulp, and it is stated that unless tension is relieved dire results follow. It is certainly more difficult to abort an infection of the pulp than to arrest cellulitis elsewhere in the hand, but this is probably due to the situation of the pulp at the end of the arterial tree of the upper limb. Premature incision for cellulitis of the pulp is thus more likely to result in extensive sloughing and may possibly cause necrosis of the terminal phalanx. It is only recently that strict immobilization of the affected hand has been insisted on, yet during this time, in several cases established infection of the pulp has subsided without operation. In others the infection has progressed to abscess formation and has yielded to simple incision, and in none has any serious complication developed.

Immobilization is secured by means of light metal or plaster splints, and swelling and congestion of the inflamed area are reduced to a minimum by elevation of the limb. This is best done with the patient in bed, but when this is impracticable the next best thing is to keep the hand near the opposite shoulder by means of a sling. The method of splinting or elevation must not interfere with the circulation, and care always should be taken that there is no possibility of this. Should operation be necessary, after-treatment should consist of the twice daily application of hot fomentations to prevent the incision from crusting over and care that the patient carries out active movements of the unaffected fingers.

There is one important point which remains, that is, the relation of disuse to the function of the hand. The hand seems to be dependent for efficiency on constant use. Complete disuse, whether produced by therapeutic immobilization or by a tender scar, is followed by atrophic changes in the fingers, which result in their disablement. This may be prevented in the former instance by discontinuing immobilization and by starting active movements as soon as healing is established. In the latter, in which the condition is more difficult to deal with, the tender area must be protected by some form of shield and the patient made to use the finger. It is important that this should be done as soon as possible; therefore, after the wound has healed, every patient is examined to determine the mobility of the fingers before he is finally discharged.

TREATMENT OF INTESTINAL OBSTRUCTION

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Recently Aird, of Edinburgh, stated that since the beginning of the century the mortality from intestinal obstruction has remained about 40 per cent. He added that despite animal experimentation, the knowledge acquired in this field has not been sufficiently applied to therapy. When one considers that intestinal obstruction is one of the most common occurrences, if not the most common, at least in the surgical clinic of Professor Delrez, and when one reflects on the high mortality reported by Aird, one is not surprised at the efforts of clinicians to improve the treatment for this grave condition.

I wish particularly to emphasize that obstruction is rarely a disease per se. It is as a rule the consequence of a preexisting condition or of a malformation, or the cause may remain obscure. But in all instances the obstruction aggravates further the original condition. One should, however, in the presence of obstruction, forget the immediate or the remote cause and employ all one's efforts to relieve the obstruction. I shall attempt to relate my conception of the treatment of intestinal obstruction and to base it, so far as possible, on physiopathologic considerations as gained from experience.

The influence of the French and the German contributions resulted in the concept that intestinal obstruction produces intoxications of various kinds. Since 1912, the American school, represented by Hartwell and Hoguet and later by Haden and Orr, whose precursors in France included such men as E. Vidal and Delore, has changed this point of view, for these men regarded death following intestinal obstruction as due primarily to anhydremia and hypochloremia. A tendency developed to ignore the toxic aspect of the problem and to consider anhydremia and hypochloremia as the only factors causing death from intestinal obstruction, at least from high intestinal obstruction. I feel that if one wishes to study all the aspects of the problem it is necessary to modify this method of interpreting the phenomena. It is much more likely that intestinal obstruction produces an intoxication first of the blood and then of the tissues. This intoxication may have several places of origin, such as the obstructed intestine or the pancreatic gland, as demonstrated by the favorable results obtained in animals when the pancreas is short-circuited, even though one cannot explain the manner in which this

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occurs. The liver likewise may have something to do with the toxic phenomena. Besides this toxemia, there develop factors of great importance, factors to which I have given the names of dehydration and demineralization of the blood and tissues. These factors alone may account partly for a particular toxemia, to the exclusion of the obstructed intestine. As a matter of fact, dehydration and demineralization result in a reduction of the volume of the blood and the arterial pressure, in consequence of which there is an alteration in the tissue circulation of the type which permits the cellular metabolites, some of which are highly toxic, to be only imperfectly removed by the blood. The result is tissue intoxication. On the other hand, the metabolites taken up by the blood are only imperfectly eliminated owing to a diminished excretion of urine, which in itself is the result of dehydration and demineralization. The result is a toxemia dependent solely on dehydration and demineralization. However, these two factors are not the only ones involved in intestinal obstruction, for if one supplies only the elements lost by dehydration and demineralization one obtains only incomplete benefit from the therapy. In order for this form of therapy to be of value, one ought to give the patient a quantity of water and of mineral elements much greater than would be necessary to make up for the losses caused by vomiting, diuresis, sweating and respiration. To recapitulate briefly, intestinal obstruction results in a toxemia, all the effects of which are made possible by dehydration and demineralization, the latter being capable in themselves of producing a part of the intoxication. I do not ignore the importance of the level of the obstruction, for I realize that the gravity of symptoms depends on its height. The intoxication, however, though obscured by the symptoms of dehydration and demineralization and not recognizable on superficial examination, remains the primary cause of the severe manifestations accompanying intestinal obstruction. The foregoing facts should serve as a guide to the choice of efficient therapy, which I shall now discuss.

TREATMENT

Certain principles in the treatment of intestinal obstruction may be considered as fundamental. If the patient's condition is not too grave and operation may be postponed for several hours, it is advisable to restore the water and minerals that have been lost. This treatment consists in furnishing the body with water in large quantities and with simple ions, particularly chlorine, sodium, potassium and calcium, in an isotonic or mildly hypertonic solution. The fluids may be administered subcutaneously or intravenously. If the condition of the patient is grave and immediate operation is indicated, this form of therapy is impossible.

Anesthesia.—The choice of anesthesia is one of the most important problems in the treatment of intestinal obstruction. One should not lose sight of the fact that the obstruction causes a toxemia, and that one should not introduce a new toxic substance into the blood stream. Local, or regional, anesthesia is the best, and it has been used in the majority of cases which I have observed at the clinic. It goes without saying that this type of anesthesia is not applicable in every case. Under certain conditions I have used spinal anesthesia, generally induced with procaine hydrochloride, with satisfactory results. I feel, however, that spinal anesthesia should not be used for the toxic patient whose arterial pressure is already very low. I shall discuss spinal anesthesia later. If local anesthesia is not sufficient, it may be supplemented with ether during the painful steps of the operation. Certain anesthetics must be used with caution. This applies particularly to anesthetics introduced intravenously or by rectum. These anesthetics when introduced into the circulation may not be well tolerated, because of hepatic changes and consequent reduction in the antitoxic function of the liver and because of diminished excretory function of the kidney. To sum up, I advise the choice of the most innocuous anesthetic, and I cannot sufficiently emphasize the advisability of local or regional anesthesia whenever possible.

Operation.—The essential principle in the treatment of intestinal obstruction is always to practice the simplest kind of operation. I have already stated that intestinal obstruction cannot be called a malady per se but is the consequence of some other preexisting lesion. It is the obstruction, however, that should always be treated. It alone constitutes an emergency. The aim of the treatment is to remove the obstruction by the simplest means. If the patient's general state permits, I treat both the obstruction and the primary cause by instituting a complete operation. Experience, however, teaches that frequently a simple operation will save a life and will permit later treatment of the causative lesion under much better conditions, while a complicated operation which relieves the obstruction and the cause results in a large number of fatalities from various complications developing a few days after the intervention. I shall refer again to the fact that the simplest operation will relieve the obstruction and that few of the patients operated on die of the effects of obstruction. However, when one practices resection and suturing of the obstructed bowel, one may expect some disagreeable complications, despite the fact that the obstruction is relieved. No tissue is less suitable for suturing than an intestine which is the seat of an obstruction. Therefore, the important principle to be applied as far as possible is to relieve the obstruction by the simplest operative technic.

Postoperative Treatment.—Frequently the most important part of the operation is the after-treatment, concerning which the following sug-

gestions are made. Rehydration and remineralization should be accomplished through injections of large amounts of isotonic or mildly hypertonic solutions of chlorine, sodium, potassium and calcium by the subcutaneous, intravenous, rectal and, if possible, oral route. This treatment has two aims, namely, to remove rapidly the toxins which tend to overwhelm the organism by instituting a satisfactory diuresis and to improve the function of the skin; in addition, the bowel functions much better when the water supply and minerals have been restored. In order for this treatment to be effective, however, one should introduce large amounts to replace the fluids lost. I have found it advantageous in some cases to wash out the stomach several hours after the operation. A certain amount of toxic material is thus removed from the gastrointestinal tract. The lavage has to be repeated only exceptionally. Symmonds advised encouraging vomiting after the operation. I prefer lavage. Some clinicians advise duodenal suction. This is an ancient method which was practiced on animals in 1767 by Monro, an English veterinarian. It was used in man by Kussmaul in 1867, with varying results. It was reintroduced by Wangensteen and Paine in 1933, and recently Paine has perfected the apparatus for aspiration. I have had no experience with this method and have not resorted to it in a single case.

I have summed up rapidly the principles which should be followed in the treatment of intestinal obstruction. I shall now describe with some detail the various forms of obstruction treated for the past six years in the surgical clinic of Professor Delrez. This experience includes 334 cases of obstruction.

MECHANICAL OBSTRUCTIONS

Congenital Stenosis and Atresia; Imperforate Anus.—A 4 day old infant with congenital atresia of the large intestine was treated by creating a fistula in the small intestine, but the child died. An infant 4 months old had imperforate anus combined with a perineal fistula, and 2 infants, each 1 year of age, had imperforate anus with a rectovaginal fistula. The treatment consisted of dilation of the anus and reduction of the rectal ampulla. The 3 infants survived, although a small rectovaginal fistula persisted in 1.

Obstruction by Foreign Bodies.—One patient had an obstruction at the level of the ileocecal valve due to undigested food. Enterostomy was performed, the intestine was emptied of its contents and the opening was closed; the patient recovered. In 1 patient the obstruction was due to ascarides. At laparotomy pressure was exerted on the bowel so that the ascarides passed on toward the cecum; the patient recovered. A sponge left in the abdomen at laparotomy was the cause of intestinal

obstruction in another patient; removal of the sponge brought about relief.

Inflammatory Tumors.—One patient with an inflammatory tumor of the cecum recovered after drainage. Another patient had stenosis due to a bacillary infection of the middle portion of the small intestine; perforation occurred, and resection with end to end anastomosis was performed. The patient died three weeks later from a pulmonary abscess. One patient with stenosis of the small intestine, caused by tuberculous infiltration of the intestinal wall, was subjected to resection and end to end anastomosis, with recovery. Another with a tuberculous cecum and complete obstruction was subjected to hemicolectomy on the right side followed by ileocolostomy and died three weeks later as a result of a pulmonary abscess. A patient with tuberculosis of the splenic flexure died twenty-four hours after simple exploratory laparotomy. Finally, a patient with obstruction of the small intestine due to a caseating mesenteric gland, 30 cm. above the cecum, was subjected to partial excision of the node; he survived the drainage but died later.

Neoplasms.—There were 2 patients with obstruction of the small intestine due to carcinomas. Resection of the tumor followed by end to end anastomosis was performed on the first patient under spinal anesthesia; death was due to peritonitis. Nothing more than an exploratory laparotomy could be performed on the second patient because of the dissemination of the cancer. Of 5 patients with tumors of the cecum, 4 were subjected to resection of the tumor followed by ileocolostomy under ether anesthesia. One of these 4 patients died of peritonitis, 1 died of pneumonia and the other 2 survived. The fifth patient survived after the creation of a fistula of the small intestine. Two patients with tumor of the ascending colon were subjected to hemicolectomy on the right side followed by ileocolostomy with recovery, though a fecal fistula persisted in 1. A third patient was treated by exteriorization of the tumor and resection. The medially placed anus was closed at a second operation, but a small fistula persisted. The three operations were performed with the patients under ether anesthesia. Six patients with carcinoma of the transverse colon were treated in the following manner: Four underwent cecostomy, 2 under local anesthesia and 2 under ether anesthesia. All 4 recovered. Two underwent resection with end to end anastomosis of the transverse colon, 1 under local anesthesia and the other under ether; 1 died of peritonitis. There were 6 patients with carcinoma of the splenic flexure. Three underwent cecostomy, 2 under local anesthesia; 2 of the 3 died later, 1 of multiple abscesses which developed in the tumor. An artificial anus was made in the transverse colon of 1 patient under local anesthesia;

death resulted from peritonitis. The 2 remaining patients were treated by exteriorization followed by extraperitoneal removal of the tumor and closure of the artificial anus. Ether anesthesia was used in 1 and procaine hydrochloride administered spinally in the other. Both recovered.

There were 20 patients with carcinoma of the sigmoid flexure. Nine were operated on under local anesthesia, 5 under spinal anesthesia with procaine hydrochloride and 1 under spinal anesthesia after the method of Jones. For 1 Schleich's anesthetic mixture was used, for 1 Schleich's mixture plus oil of cajeput, for 1 ether and for 1 chloroform.

The following types of operations were performed: creation of an iliac anus, 10 cases; exteriorization and removal of the tumor, 4 cases; exteriorization and extraperitoneal removal of the tumor with closure, 3 cases; exteriorization and intraperitoneal removal of the tumor with closure, 2 cases, and creation of a fistula in the terminal portion of the ileum, 1 case.

Seven of the patients in whom an iliac anus was made died between the eighth day and the third month after the operation; 2 of those on whom exteriorization was performed died between the fourth and the fifteenth day.

There were 49 patients with cancer of the rectum. Thirty-six were operated on under local anesthesia and 1 under spinal anesthesia with procaine hydrochloride. For 10 ether was used, for 1 Schleich's mixture plus oil of cajeput and for 1 a preparation of ethyl chloride locally.

A simple iliac anus was created in 29 cases; an iliac anus was created followed by sacroperineal resection in 15 cases, and abdominal perineal resection was done in one stage in 5 cases.

Six of the patients in whom an iliac anus was made died between the third day and the third month after the operation, from various causes. Four of those subjected to abdominal perineal resection died from one to ten days after intervention.

Membranous Enterocolitis.—Of 2 patients with membranous enterocolitis, 1 recovered on medical treatment and the other died of peritonitis five days after cecostomy.

Duodenal Obstruction.—In 1 patient who had undergone gastroenterostomy for a gastric ulcer obstruction caused by the trunk of the mesenteric artery developed at the junction of the superior two thirds and the inferior third of the duodenum. Duodenojejunostomy was performed with the patient under ether anesthesia, and death occurred on the fifteenth day.

Obstruction Due to Adhesions.—There were 4 patients who had adhesions of congenital origin. In 1 compression of the intestine was

caused by a branch of the mesenteric artery, which produced anemia of the intestinal loop and a consequent obstruction. There was 1 patient with obstruction due to Meckel's diverticulum and 13 with obstruction due to postoperative adhesions (following appendectomy, operation for perforated ulcer, hysterectomy and operation for strangulated hernia). Twelve of the patients were treated by division of the adhesions, 1 by division of the adhesions and drainage, 3 by enterostomy and 1 by side to side anastomosis. One patient was kept on a milk and ice cream diet.

Two of the patients died after division of the adhesions, 1 after division of the adhesions and drainage and 1 after side to side anastomosis.

The most favorable operation, without doubt, is that of a simple division of the adhesions. However, it is not always sufficient and must be supplemented by anastomosis or resection followed by anastomosis, which makes the prognosis more grave. In certain cases the adhesions cannot be divided and one has to be satisfied with enterostomy either on the loop just above the obstruction or more frequently on the first presenting loop. This operation may be radical. After the release of the intestine and relief of the obstruction, detoxification of the patient is instituted and the fistula closes spontaneously or is closed by the surgeon. More frequently the obstruction persists. On rehydration of the patient, the fistula may close spontaneously. More frequently the obstruction may be removed by operation when the patient's state has improved. If the obstruction persists, a second enterostomy is performed in order to improve the general state of the patient, and the obstruction is later treated operatively. In any event, an enterostomy is not the most satisfactory procedure, but it enables one sometimes to save the life of a patient who could not withstand a severe operation.

I shall add to this group of cases those of intestinal obstruction due to bacillary peritonitis, of which there were several. Nine patients with fibrous adhesive peritonitis were treated in the following manner: 1 by ultraviolet irradiation, 4 by simple laparotomy, with 2 deaths; 1 by laparotomy, drainage and roentgen irradiation, with the development of a stercoraceous fistula and death after two and one half months; 1 by laparotomy, drainage and ultraviolet rays; 2 by laparotomy and freeing of the adhesions and 1 by laparotomy, freeing of the adhesions and ultraviolet irradiation.

Nine patients with peritonitis of the ascitic type were treated in the following manner: 1 by simple heliotherapy; 4 by laparotomy and exposure to air, with 1 death; 1 by laparotomy, exposure to air and peritoneal lavage with oil of cajeput; 2 by laparotomy, drainage,

exposure to air and postoperative treatment with ultraviolet irradiation and 1 by laparotomy, exposure to ultraviolet rays during the operation and postoperative treatment with ultraviolet rays.

Obstruction Due to Compression of the Intestine.—There was 1 patient with obstruction of the splenic flexure caused by hypertrophy and ptosis of the spleen. The obstruction was removed by splenectomy. Two patients with obstruction in the course of pregnancy were subjected to exploratory laparotomy, after which the obstructive phenomena disappeared.

Strangulated Hernias.—There were 141 patients with strangulated hernia, including those of the inguinal, femoral, umbilical, epigastric and ventral types. One hundred and twenty-five of these were adults between 16 and 87 years of age, and 16 were infants from 5 months to 5 years of age. The duration of the strangulation varied from four and one-half hours to seven days. Taxis was practiced on 10 adults and 1 infant. One death occurred on the sixth day, from cerebral hemorrhage with uremia. The results in another case were very instructive. After an unsuccessful attempt was made for about twelve minutes to reduce the hernia by taxis, an operation was decided on, and spinal anesthesia was induced with procaine hydrochloride. Before the operation the hand was placed over the hernia, and mild compression of the hernial contents resulted in their reduction. The patient no longer experienced any pain. It was decided not to operate. On the following day pains returned. Laparotomy revealed a properly reduced hernia with one intestinal loop badly injured and perforated. The patient died. This accident emphasizes that one should be very cautious in the practice of taxis. I did not consider the efforts employed sufficiently rough to cause perforation of the intestine. On the other hand, the strangulation did not last more than three hours and I had every reason to believe that the vitality of the intestine was not compromised. There was no reaction of any kind in the vicinity of the strangulation. It is probable that the spinal anesthesia caused relaxation of the abdominal wall and permitted the reposition of the intestine, which perforated later. Leriche stated that although intestinal obstruction may be relieved by spinal anesthesia, such relief is not to be relied on. I shall speak of this later. Another disadvantage of the method of taxis consists in the possibility of reducing the hernia en masse. It permits of the continuation of obstruction and only delays the operation. To sum up, one should be extremely careful in performing taxis.

One hundred and thirty patients with strangulated hernia were subjected to operative intervention. Thirteen infants were operated on under ether anesthesia and 2 under chloroform. Nine adults were

operated on under ether anesthesia, 2 with chloroform, 1 under Schleich's anesthesia and 1 with Schleich's mixture plus oil of cajeput. The remaining 106 patients were operated on under local anesthesia induced with 1 or 0.5 per cent procaine hydrochloride in amounts of from 30 to 50 cc.

I have employed, as a rule, a very simple technic, the Bassini or the Forgue method for inguinal hernia, Ruggi's method for femoral hernia and a simple reenforcement of the abdominal wall for umbilical or epigastric hernias or eventrations. The intestine, even though considerably altered, assumes a rosy coloration and manifests a few contractions after the application of warm physiologic solution of sodium chloride and is then returned to the abdomen. Of 28 patients operated on for this condition, 5, all adults of advanced age, died. One had a strangulated femoral hernia of five days' standing with a beginning gangrene of the bowel and intestinal paralysis; another had a femoral hernia of twenty-four hours' duration and died ten days later from pulmonary abscess; another patient died as the result of acute pulmonary edema; the fourth died of peritonitis despite the fact that the bowel did not appear much altered at the time of operation, and, finally, the fifth died from an unknown cause. In 10 cases a complicated procedure was carried out: In 2 instances the perforated herniated intestinal loop was sutured and the patients recovered. In 1 case the loop was sutured and attached to the neck of the sac. In 1 case the intestinal loop was exteriorized and resected; the two lumens were sutured to the skin, end to end fashion; death took place after twelve days. In 4 instances enterostomy was performed on an exteriorized bowel; 3 patients died, and 1 recovered with a fistula, which was later closed. Twice resection of the loop and intestinal anastomosis was practiced; in both instances the patient died.

It is evident that the simple operations offer a greater chance of saving the life of the patient with a strangulated hernia than the complicated operations, which are followed by a considerable mortality. Finally, I wish to mention 1 case of strangulated hernia in which phenomena of obstruction developed one month later as a result of a plastic peritonitis and which necessitated intestinal resection. The patient recovered.

Volvulus.—There were 4 patients with volvulus. One, a 4 day old infant with volvulus of the small intestine, resulting in necrosis of the loop, underwent resection with an end to side anastomosis which proved fatal. Two patients with volvulus of the cecum, of the ascending colon and of the sigmoid flexure in whom untwisting was performed recovered. Finally, the last patient was admitted to the clinic in a moribund condition as a result of volvulus of the ascending colon. No treatment was attempted.

Intussusception.—There were 10 patients with intussusception. In 2 the small intestine was involved; in 1 resection followed by an end to end anastomosis was successfully practiced. The other patient died. Autopsy revealed a reduced intussusception followed by fixation of the loop to the parietes. Seven patients with ileocolic intussusceptions were operated on. For 5 ether anesthesia was used, for 1 chloroform and for 1 Schleich's mixture plus oil of cajeput. Reduction of the intussusception followed by ileocolopexy was practiced. In 1 case a simple reduction was done. One death resulted from hyperthermia. One patient survived after the reduction of a colocolonic invagination. In 1 case of ileocolic invagination an attempt at reduction was made by means of an enema of barium sulfate. The invagination was successfully reduced, but it recurred two days later and operation was necessary. The principle of this method is old. It originated, as a matter of fact, with Hippocrates, who practiced it in the treatment of intussusception and particularly of certain forms of intestinal obstruction. He recommended introduction into the anus of large quantities of air by means of a sound or a tube, and when the abdomen became sufficiently distended the tube was removed and water was introduced immediately after. Hippocrates claimed to have brought about a cure in that fashion in many cases of invagination.

I have recorded 55 fatalities among 302 patients with mechanical obstruction, a percentage of 18.25, which is a relatively small mortality. I particularly emphasize the fact that the cause of death in the majority of instances was not the obstruction. All patients operated on, with the exception of 4 or 5, were relieved of the obstruction in the course of the operation, with reestablishment of the fecal current, death supervening as a result of various conditions, some of which were undoubtedly favored by the obstruction. On the other hand, a study of the postoperative deaths in the cases of carcinoma of the sigmoid flexure and of the rectum and above all in the cases of strangulated hernia, reveals that the safety of the patient lies in the less complicated operations. Therefore, in the presence of a mechanical obstruction of the intestine the first concern should be that of saving the life of the patient. One should not resort to complicated operative procedures but should postpone the removal of the cause of the obstruction to the time when the patient has been relieved of his toxemia, anhydremia and loss of minerals.

FUNCTIONAL OBSTRUCTIONS

Functional obstructions present an entirely different story. First, the etiologic factors are unknown in most of the cases, and even if under certain conditions the primary cause of ileus is found, it is impossible to establish the relation of cause and effect. This lack of knowledge is due to ignorance concerning the role of the innervation of the

intestine in man. Neither the physiologists nor the clinicians possess an accurate idea of the physiology of intestinal innervation. The methods of study have not been effective. By one of the methods a small portion of the intestine is removed from an animal or from a human being and placed in a nutritive solution or is nourished by defibrinated blood with the addition of different chemical substances. Such a method cannot possibly give one any idea of the conditions *in vivo* or *in situ*, either in the normal state or under pathologic conditions, and cannot be used to elucidate the physiology of intestinal innervation. The only permissible method is to study the bowel *in situ* or in a living animal, and here one immediately runs into insurmountable difficulties. If one wishes to investigate the role of innervation of the intestine one should theoretically be able to deprive this viscus of its nerve supply. It can readily be seen that this cannot be accomplished, because it implies the removal not only of the sympathetic trunks and the pneumogastric and the intermediary ganglionic plexuses but of the intramural plexuses of Auerbach and Meissner. It can readily be understood that such a performance is impossible and that because of the autonomic character of the bowel complete denervation cannot be obtained. Lack of knowledge relative to the role of innervation of the intestine in the normal or pathologic state is responsible for the uncertainty in which one finds oneself when considering the field of paralytic ileus from a pathologic standpoint. Moreover, mechanical obstructions may be complicated by functional phenomena. Occasionally in strangulated hernias an entire loop of intestine is not found in the hernial sac, but only a piece of compressed omentum or a small pinched-off portion of the lateral antimesenteric border of the intestine. I have seen 2 cases in which the lumen of the entire intestine was patent and in spite of it there existed an obstruction which disappeared when the omentum was released or when the lateral pinching was removed. The remarkable thing in such cases is the total obstruction such as follows strangulation of the entire loop. This observation makes it probable that there exist centripetal influences concerning the intestinal innervation, in spite of the fact that this is contradicted by certain physiologists.

I shall consider briefly a few examples of functional ileus that I have observed. I have stated that mechanical obstruction is, as a rule, secondary to some preexisting condition. Only when an obstruction is produced is one compelled to turn one's attention to the original cause, and one should attempt to remove the obstruction before anything else. Functional ileus may likewise be secondary to an original condition, but in a great number of cases it is the latter which presents all the signs and the treatment of which results in the amelioration or cure of the condition. Such is the case with obstructive phenomena

which accompany inflammatory processes of the abdominal viscera (appendicitis, cholecystitis, salpingitis, pancreatitis, perforation of an ulcer, renal diseases).

I shall not discuss these forms of obstruction here. With these conditions, therapy is directed to the cause.

Inflammatory Obstructions.—Obstructions of this type are secondary to peritonitis and develop some time after an abdominal condition. I have observed 2 cases of peritonitis secondary to perforation of an ulcer. Drainage was established in 1 case, and the patient died six days later; in the other case the patient received symptomatic treatment only and died at the end of twenty-four hours. In 3 cases peritonitis followed appendicitis of several days' standing for which operation had not been performed. The treatment consisted of appendectomy and drainage. The patients recovered. I have had 7 patients between the ages of 57 and 85 who presented blood urea concentration of from 1 to 6 Gm. per hundred cubic centimeters. Only 1 patient survived and for this one the treatment consisted of restoration of the fluids and minerals on a massive scale. The other 6 patients were treated as follows: Three were subjected to an exploratory laparotomy, 1 to the establishment of an iliac anus and 2 to lavage combined with extensive bleeding. All died between forty-eight hours and twenty-eight days after the institution of treatment. The exploratory laparotomies revealed general dilatation of the entire intestine without any obstruction to the fecal current. I believe that the patients died not from the obstruction but from uremia, since in the majority of the patients treated the fecal current was reestablished. I feel that the best treatment for this obstruction is copious rehydration and remineralization.

Lead Poisoning.—Two patients suffering from saturnism presented functional spastic obstruction. They recovered with treatment of the saturnism by removal of the lead and administration of a milk diet and potassium iodide.

Coronary Thrombosis.—A patient suffering from coronary thrombosis of the anginal type presented genuine complete paralytic obstruction. The obstruction was relieved by enemas and hot applications. Four days later the patient suffered another attack of angina and died. Postmortem examination revealed an infarct of the myocardium.

Intestinal Worms.—One patient presented a functional intestinal obstruction of the spastic type, which was found to be due to intestinal parasites. The obstructive crises disappeared in the course of treatment. Perhaps this obstruction was of the type described by Rost and attributed to substances secreted by the genital and digestive organs of the parasites and producing a condition of the bowel. The treatment directed toward the removal of the parasites was followed by the disappearance of

obstructive crises, but nothing justifies my saying that the relation exists between the worms and the obstruction.

Acute Alcoholism.—A patient presented characteristic symptoms of intestinal obstruction following a drunken orgy. The use of enemas and a diet gave relief.

Tabes.—A patient suffering from tabes and subject to obstructive phenomena of paralytic nature was subjected to an exploratory laparotomy, which failed to reveal the existence of any lesion. The crises disappeared after antisyphilitic treatment.

Hysteria.—Two hysterical patients presented symptoms of paralytic obstruction. Treatment of their nervous manifestations was effective in curing the obstruction.

Functional Ileus of Unknown Cause.—In 12 patients I observed intestinal obstruction of spastic or of paralytic nature; at times the spastic and the paralytic phenomena alternated. I have searched in vain for the cause of this type of obstruction. One patient had a thrombosis of the left external iliac vein. The rest of the patients presented nothing abnormal but the obstruction. Seven patients were treated medically by enemas and laxatives, with recovery. Five were subjected to operation. The 3 who underwent exploratory laparotomy died in from twenty-four hours to seventeen days after the operation. One patient on whom cecostomy was performed, and another on whom enterostomy of the small intestine was done died twelve and fifteen days later, respectively, in spite of the fact that the obstruction was relieved. To sum up, there were 9 deaths in 32 cases of functional obstruction, or 28 per cent. It appears that one should be careful about operating in cases of obstruction which is the result of peritonitis. Operative intervention on uremic patients with obstruction or on patients with functional obstruction of unknown cause gave bad results, despite the fact that the intervention was no more than an exploratory laparotomy or an enterostomy. The best therapy for this type of obstruction is conservative—diet, enemas and above all the administration of fluids and minerals. At the beginning of the discussion on functional ileus I emphasized that precise knowledge regarding intestinal innervation is very meager. I wish to state that even though I have classified the obstructions in cases of uremia, of lead poisoning, of coronary disease, of infection due to intestinal parasites, of acute alcoholism, of tabes and of hysteria, I do not know whether a relation exists between these conditions and the obstruction. All I wish to state is that an obstruction manifested itself in subjects affected with these diseases, and in view of the fact that no cause for the obstruction could be found I feel that it is wise to treat the obstruction in a symptomatic manner concomitantly with the disease itself. Since treatment of the general cause favorably influences the

obstruction, it is possible that there is a relation between the general disease and the obstruction. In any event, the relation is uncertain.

This is obviously not the case in functional ileus associated with peritonitis. It is probable that the peritoneal infection itself is capable of causing intestinal paralysis by action on the nerves and plexuses. Again, peritonitis acts directly on the muscle fibers of the intestine. The study of the muscular layers of the bowel in cases of peritonitis discloses considerable edema of the muscular fibers and of the tissues between the fibers as a result of the infection or of the hyperemia of the bowel. Surgical treatment in these cases should be regarded in various aspects. The principle of the treatment is to drain the peritoneal cavity. If this proves inefficient, one has to resort to enterostomy; the opening may close spontaneously or may have to be closed after recovery. In all of the cases this treatment can be efficiently supported by massive rehydration and remineralization.

POSTOPERATIVE ILEUS

This is a particular form of ileus, either paralytic or spastic, which may follow any operative intervention but most frequently follows an abdominal operation. This should not be confounded with postoperative ileus with obstruction which follows an abdominal operation. The latter is also of a paralytic nature but depends on a more or less severe peritoneal reaction; it belongs in the domain of the functional obstruction consecutive on peritonitis. I am speaking here of a postoperative ileus without any sign of peritoneal reaction. The cause of this condition is unknown, and for its treatment I have used lavage of the stomach, duodenal suction, hot applications to the abdomen and warm and cold enemas. The most satisfactory procedure is lavage of the stomach; the rest of the procedures gave favorable results in some of the cases but in others the results were uncertain. One can employ pharmaceutical products. I have experimented with many preparations, none of which proved very satisfactory regardless of whether their action was based on experimental or on clinical experience. Included in this group were posterior pituitary extract, peristaltin (a glucoside of *Cascara sagrada*), acetylcholine, physostigmine, atropine, opium and numerous other commercial preparations. In some of the cases this treatment was followed by the passage of gases and feces, but in the majority of cases the drug proved inefficacious, so that the actual effectiveness of these products remained problematic. As a result of experimental work, morphine has been employed in recent years to reestablish the intestinal peristalsis. In my experience this therapy has not given the results which were expected of it.

Intravenous Injections of Hypertonic Solutions.—Postoperative ileus is sometimes treated with injections of hypertonic solutions. From 10 to 20 per cent solutions of sodium chloride are most frequently employed. Introduced into a vein in a dose of 20 cc., such a solution will provoke a violent peristalsis and will relieve postoperative paralysis. Delrez and Orban have found this method inefficient in 66 per cent of cases of postoperative ileus, and these figures are confirmed every day. It is certain that the injection of a 20 per cent solution of sodium chloride may sometimes rapidly relieve the paralysis of the intestine and be followed by evacuation of feces and gases in a short while, but the untoward phases of this treatment are numerous and I feel that it is not the ideal treatment of postoperative ileus. Other hypertonic solutions were tried in man and the animal (sodium citrate, urea and dextrose) with results comparable to those obtained with hypertonic solution of sodium chloride. I emphasize once more that intravenous injection of hypertonic solution of sodium chloride should not be employed in cases of mechanical obstruction. Four years ago I stated that this treatment is not efficacious and is, in fact, dangerous, and only recently Aird expressed the same view. Some clinicians resort to the employment of enemas of a 20 per cent solution of sodium chloride in cases of paralytic ileus. I have not had any experience with this method, but I feel that it is probably not superior to those I have mentioned.

Spinal Anesthesia.—Leriche appears to be the first to have advised spinal anesthesia for the treatment of paralytic ileus (1912). Since then the method has been rapidly popularized. Wagner, Bonniot and Bartlett gave different explanations of its action, but these are incomplete and inadequate. Numerous publications emanating from the Surgical Society of Paris in 1927 make this method appear well founded, and I have observed that patients have a prompt evacuation a few minutes after the injection of a spinal anesthetic. However such a result is not always attained, and the method may result in regrettable accidents, as pointed out by Leriche himself. It is preferable, therefore, to use caution in employing spinal anesthesia for the relief of the paralytic postoperative obstruction and not to expect too brilliant results.

CONCLUSION

All the methods which I have mentioned for the treatment of postoperative ileus can be employed for any paralytic ileus. I feel, however, that some of them should not be used if the intestinal paralysis is due to an inflammatory peritoneal reaction. The aim of these methods is to provoke intestinal peristalsis, but since the peritoneal exudate should not be spread, I feel that it is best in cases of peritonitis to keep the bowel at rest.

In conclusion, I wish to say a few words about the therapy I regard as the most effective against postoperative ileus. In the greater number of cases this complication develops in a patient who previous to the operation was already in a state of dehydration and demineralization as a result of the malady which indicated the operation (vomiting, withholding of food, profuse sweating and diarrhea), or a similar state of dehydration and demineralization develops after an operation, owing to causes comparable to those just mentioned, to which should be added evaporation and hemorrhage during the operation. To sum up, postoperative ileus is produced as a result of loss of water and minerals, and the best means of preventing this complication consists in administering a satisfactory supply of fluids and minerals after surgical intervention. This is a most important preventive aspect of the problem. If despite everything postoperative ileus ensues, the best treatment is that of supplying massive doses of fluids and minerals. I believe that this furnishes a satisfactory explanation for the good results obtained by Dubois de Genève by blood transfusion in cases of postoperative ileus. It amounts to no more than a special form of supplying of water and minerals with its active antitoxic effects. Of all the therapeutic measures in the treatment of intestinal obstruction, rehydration and remineralization give the most satisfactory results. In certain exceptional cases all the means which were employed failed. In such cases one must employ a method, unpleasant though it may be, which may save a few lives, and perform an enterostomy, the effect of which is comparable to that which I have mentioned in cases of obstructions due to adhesions.

SPREADING PERITONITIS COMPLICATING ACUTE PERFORATIVE APPENDICITIS

EXPERIMENTAL STUDIES

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Approximately 300,000 persons in the United States will be operated on this year for acute appendicitis and its complications. Twenty thousand of these will die at an average age of 27 years. Fewer than 2,000 will die of acute appendicitis. More than 17,000 will die of peritonitis.

Of the 300,000 persons operated on, nearly 195,000 will have an intact appendix; the serous coat will be unruptured. The mortality will be less than 1 per cent. Of the 300,000, it is estimated that 105,000 will have peritonitis at the time of their admission to the hospital and approximately 1 of every 6 of these will die; 63,000 will have local peritonitis and approximately 3 per cent, or 1 in 30, will die; 42,000 will have spreading peritonitis and more than 15,000, or 1 in every 3, will die. Over 80 per cent of those who die will die of spreading peritonitis.

During the past six years our attention in the Department of Surgical Research, Temple University Medical School, has been focused on spreading peritonitis complicating acute perforative appendicitis. We have produced in dogs a form of spreading peritonitis which clinically, pathologically and from a bacteriologic and serologic point of view, closely resembles that seen clinically following acute perforative appendicitis. The bacteriologic findings are reported separately elsewhere.

INDUCTION OF SPREADING PERITONITIS IN DOGS

Selection of Animals.—The dogs were selected at random, except that the control dogs and the treated dogs were of approximately equal size and weight. Pregnant animals and animals weighing less than 4.5 Kg. were not used. No effort was made to prepare the dogs except that they were not fed on the morning of the operation.

Operative Technic.—The operation was performed with the dog under ether anesthesia. The abdomen was shaved, scrubbed with ether and painted with a 3.5 per cent tincture of iodine. Strict aseptic precautions were observed. A

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right rectus incision about 10 cm. long was made; the appendix was located, drawn up and dissected free of its mesenteric attachments, and all bleeding vessels were clamped and separately ligated with fine silk. A double ligature of silk was then tied tightly about the appendix as close to its base as possible. After inspection to make sure that hemostasis was complete, the abdominal contents were replaced and the wound was closed in layers, silk being used throughout. The fascia was reenforced with interrupted sutures. Drains were not used. During the operation precautions were taken to prevent the escape of blood into the peritoneal cavity. No dressing was applied.

Administration of Laxatives.—Early in the investigation it was found that by giving 30 cc. of castor oil to the average dog twenty-four hours after separating the appendix from its mesentery and ligating the blood vessels and the appendix at its base it is possible to induce spreading peritonitis. Table 1 shows that the mortality in this series of experiments was 68.52 per cent. Ninety-one and nine-tenths per cent of the deaths were caused by spreading peritonitis.

The next step was to give 30 cc. of castor oil to a group of animals directly after the operation. The mortality rose to 78.28 per cent, and 94.45 per cent of the dogs died of spreading peritonitis (control group *B*). An average dose of 54.1 cc. of castor oil was then administered to a third group of dogs directly after the operation. The mortality rose to 91.87 per cent, and 100 per cent died of spreading peritonitis (control group *C*).

Comment.—The results in control groups *A* and *B* prove that the time of administration influences the outcome, and the results in control group *C* show that the quantity of laxative administered also influences the outcome. Every animal that died after receiving 2 ounces of castor oil following the operation died of spreading peritonitis.

Postoperative Care.—The dogs were placed in metabolic cages and allowed to recover before being returned to the animal house. Food and water were placed before them. They were disturbed only when brought to the operating room for the administration of laxatives or for other treatment. They were returned to the animal rooms as rapidly as possible, with as little handling as possible. Special care was taken not to squeeze or massage the abdomen.

In the animal rooms no special precautions were taken except that the dogs were kept segregated in individual cages. The rooms were heated during the coldest weather only, the room temperature never being higher than 50 F. except when the weather made it so.

Postmortem examinations were carried out in all instances as soon as possible after death. If an autopsy was not performed to determine the cause of death, if the animal died of pneumonia or of some other complication within ten days, or if at a subsequent operation the appendix was found to be intact, showing that the ligature had slipped, the animal was discarded.

TREATMENT OF SPREADING PERITONITIS IN DOGS

Although 323 dogs were used, 58 of this number are not included in the control or treatment groups. The normal postoperative recovery

period of 18 of the 58 dogs was interrupted by another operation to obtain material for bacteriologic and histologic examinations. A number of these dogs recovered and were used subsequently as donors for blood transfusions and as donors of convalescent serum.

Thirteen animals died of the effects of the anesthetic before, during or immediately after the operation. Most of these deaths occurred in the early stages of the work. In 14 animals the ligature placed around the base of the appendix was not drawn sufficiently tight and became loose directly after the operation, or the mesentery was not completely separated from the appendix and gangrene of the appendix did not develop. Subsequent exploration of the abdomen in each instance revealed a normal appendix with no evidence of local or spreading peritonitis. Eleven animals were excluded because of delay in carrying

TABLE 1.—*Results of Administration of Castor Oil*

Control Group	Number of Dogs	Average Weight, Kg.	Laxative (Castor Oil), Cc.	When Given	Lived	Died	Mortality, Per-centage	Average Duration of Life of Dogs That Died, Hr.	Pathologic Picture*	
									S. P.	L. P.
A	54	9.5	30	24 hr. after operation	17	37	68.52	67.24	91.90	8.10
B	23	9.26	30	Immediately after operation	5	18	78.28	61.95	94.45	5.55
C	12	9.4	54.1	Immediately after operation	1	11	91.67	66.00	100.00	0.00
Summary	89	9.38			23	66	74.16	65.35	93.93	8.07

* In this table and in the following ones S. P. indicates spreading peritonitis; L. P., local peritonitis.

out postoperative treatment or because of accidents. One dog died of hemorrhage, and in 1 case autopsy was incomplete.

Of the 265 dogs used, 158 received treatment for spreading peritonitis. Eighty-nine were used as controls and 18 for bacteriologic and histologic investigations. Control groups are designated A, B and C. Treatment groups are numbered 1, 2, 3, 4, 5, 6, 7, 8 and 9.

As the results of our bacteriologic investigations indicated the presence of anaerobes and especially of *Clostridium welchii*, it was decided to use *Bacillus perfringens* antitoxin in the treatment of induced spreading peritonitis in dogs, and our attention was directed toward determining the optimum dose and time of administration.

In treatment group 1, the administration of moderate doses of *B. perfringens* antitoxin intramuscularly reduced the mortality from 68.52 per cent (control group A) to 36.36 per cent. By increasing by 80 per cent the amount of laxative administered, the mortality was increased to 91.67 per cent (control group C); but this mortality was reduced in a group similarly prepared to 28.66 per cent—a decrease in the mortality percentage of 85.01 and a reduction in mortality of 70.9 per cent—by an improvement in the method of administration of the antitoxin (treatment group 2).

The question arose whether or not the intravenous injection of antitoxin would further reduce the mortality. To determine this, the antitoxin was given to a group of dogs prepared similarly to control group *B*. In this group, the animals, after having had the mesentery separated from the appendix and the base of the appendix ligated, received 30 cc. of castor oil directly after the operation. In the control group the mortality was 78.26 per cent; in the treatment group, after the intravenous injection of *B. perfringens* antitoxin, the mortality was reduced to 63.16 per cent—a decrease in the mortality percentage of 15.12 and a reduction in mortality of 19.3 per cent (treatment group 3).

COMMENT ON THE DOSE OF *B. PERFRINGENS* ANTITOXIN

Table 2 shows the amounts of *B. perfringens* antitoxin given intramuscularly per kilogram of body weight, together with the mortality and the average postoperative duration of life of the dogs that died.

TABLE 2.—Results of Administration of *B. Perfringens* Antitoxin in the Treatment of Spreading Peritonitis

Treatment Group	Number of Dogs	Average Weight, Kg.	Laxative (Castor Oil), Cc.	When Given, Hr. After Operation	Antitoxin, Cc.	Average Dose, per Kg., Cc.			Mortality, Percentage	Average Duration of Life of Dogs That Died, Hr.	Pathologic Picture		
							Lived	Died			S. P.	L. P.	P.
1	44	8.74	30.00	24	28.48	3.35	28	16	36.36	88.56	77.72	27.28	
2	15	9.40	57.66	24	29.10	3.10	11	4	26.66	118.00	50.00	50.00	
Summary of intramuscular antitoxin groups	59	8.90	26.00	3.21	39	20	33.90	
Treatment group 3 (antitoxin, intravenous)	19	8.50	30.00	Immediately	42.10	4.95	7	12	63.16	76.00	83.33	16.67	

Group 1 is made up of the dogs that first received antitoxin. The amount given was small, moreover, as 43.18 per cent of the dogs received only one dose, 3.64 per cent received two doses and 43.18 per cent received three doses. The dogs that recovered received an average amount larger by 77 per cent than the dose given those that died. The average postoperative duration of life of the dogs that died in group 3 was eighty-eight and one-half hours. No death occurred in less than forty-eight hours. Nine of the 16 dogs that died could have received a second dose and 5 a third dose of antitoxin. The dose of antitoxin in cubic centimeters per kilogram was slightly larger for group 1 than for group 2. In group 2, both the dogs that survived and those that died received approximately the same amount of antitoxin.

From the standpoint of mortality and the lengthened duration of life of the dogs that died after the operation, the results in group 2 are

remarkable, especially when it is realized that the dogs in this group received doses of laxative averaging 89 per cent larger than those given to group 1.

At this point in our investigation the question was raised how much, if any, of the reduction of mortality achieved by the use of *B. perfringens* antitoxin was due to the antibodies present in normal horse serum, the vehicle for the *Cl. welchii* antitoxin. To determine this, a group of 20 dogs (treatment group 4) was treated with normal horse serum injected intramuscularly, spreading peritonitis having been induced in the manner previously described. At this point it may be stated, to avoid repetition, that the operative technic was precisely the same for all dogs in both control and treatment groups, the only variable factor being the time of administration and the amount of castor oil given.

The results obtained with horse serum are shown in table 3.

TABLE 3.—*Experimental Group 4—Horse Serum*

Number of Dogs	Average Weight, Kg.	Laxative (Castor Oil), Cc.	Horse Serum, Cc. (Average)	Lived	Died	Mortality, Per-centage	Average Duration of Life of Dogs That Died, Hr.	Pathologic Picture	
								S. P.	L. P.
20	9.63	37.5	27.3	8	12	60	80.3	91.67	8.33

The administration of horse serum reduced the mortality 12.43 per cent and increased by nearly thirteen hours the average duration of life of the dogs that died after the operation. The percentage of dogs that died from spreading peritonitis was increased 1.4 per cent.

Since *B. perfringens* antitoxin seemed to control satisfactorily the toxemia produced by *Cl. welchii*, we felt it might be advantageous to combine other antisera or whole blood with the antitoxin in order to control the effects of other organisms, especially of *Bacillus coli* and of *Streptococcus*.

Before instituting the combined treatments for spreading peritonitis, we decided to determine the effect of whole blood alone, given intravenously.

Each of a group of 18 dogs was given a total average dose of 179.83 cc. of whole blood (not immunized); approximately 60 cc. was given on the day of the operation and the same amount on the second and third days after the operation. The mortality in this group (treatment group 5) was 91.66 per cent, and the average postoperative duration of life of the dogs that died was sixty-three hours. In treatment group 6, injections both of whole blood and of *B. perfringens* antitoxin were given. As the average weight of the dogs used in this experiment was greater the amount of blood was increased accordingly.

each dog receiving a total average dose of 206 cc. on consecutive days. The dose of perfringens antitoxin injected was 4.83 cc. per kilogram of body weight. The mortality in this group was 33.33 per cent; the average postoperative duration of life of the dogs that died was sixty-seven and one-half hours. The results in the experiments on dogs of these two groups are summarized in table 4.

In both these groups the laxative was administered immediately after the operation.

The dogs in treatment group 7 received immune serum in addition to *B. perfringens* antitoxin. This serum was obtained from dogs that had received antitoxin and had recovered from induced spreading peritonitis following rupture and gangrene of the appendix. The dose of antitoxin injected was 4 cc., and

TABLE 4.—*Treatment Groups 5 and 6—Transfusions*

Treatment Group	Number of Dogs	Average Weight, Kg.	Laxative (Castor Oil), Cc.	Treatment			Lived	Died	Mortality, Percentage	Average Duration of Life of Dogs That Died, Hr.	Pathologic Picture	
				B. Perf. Ant., Cc.	Whole Blood, Cc.						S. P.	L. P.
5	12	9.46	30	0	179.83		1	11	91.66	63.12	91	9
6	12	11.18	30	54	206.00		8	4	33.33	67.50	100	0

TABLE 5.—*Treatment Groups 7, 8 and 9*

Treatment Group	Number of Dogs	Average Weight, Kg.	Laxative (Castor Oil), Cc.	B. Perf. Ant., Cc.	Additional Cc.	Lived	Died	Mortality, Percentage	Average Duration of Life of Dogs That Died, Hr.	Pathologic Picture	
										S. P.	L. P.
7	12	14.17	30	56.66	Immune blood serum 52.17	8	4	33.33	96	100	0
8	12	11.11	30	24.66	Polyvalent <i>B. coli</i> serum 24.66	8	4	33.33	72	100	0
9	12	9.35	30	0	Immune blood serum, lyophilized 70	9	3	25.00	48	100	0

that of immune serum 3.72 cc., per kilogram of body weight. The mortality in this group was 33.33 per cent, but the average postoperative duration of life of the dogs that died was increased to ninety-six hours, which is longer than any of the treated dogs lived except those in group 2.

The dogs in treatment group 8 received polyvalent *B. coli* serum in addition to *B. perfringens* antitoxin. The dose of antitoxin was 2.18 cc., per kilogram of body weight. The mortality was 33.33 per cent, and the average postoperative duration of life of the dogs that died was seventy-two hours.

The dogs in treatment group 9 received lyophilized immune blood serum given intramuscularly. The average amount given to each animal was 70 cc. per kilogram of body weight. The mortality was 25 per cent; the average postoperative duration of life of the dogs that died was forty-eight hours (table 5).

The dogs in all these groups received the laxative immediately after operation.

COMPARISON OF RESULTS OBTAINED IN DIFFERENT
GROUPS OF ANIMALS

The difference in the average weights of dogs in the two groups, 0.15 Kg., is a negligible factor. The average dose of castor oil given to the treatment groups exceeded that given the control groups by 1.22 cc. While this is a small average increase, in the aggregate it amounts to 129.32 cc., and any effect it might have would be unfavorable to the survival of the dogs in the treatment group, because of the greater likelihood of increased peristalsis, which makes localization more difficult. The postmortem examinations which were made in over 95 per cent of

TABLE 6.—*Comparison of the Results Obtained in the Control Groups and the Different Treatment Groups*

Groups	Number of Dogs	Mortality, Percentage	Average Duration of Life of Dogs That Died, Hr.	Pathologic Picture: Spreading Peritonitis
Control groups, A, B, C.....	89	74.16	65.35	93.93
Treatment groups 1 and 2, B. perfringens antitoxin (intramuscularly)	59	38.89	94.40	66.67
Treatment group 3, B. perfringens antitoxin (intra- venously)	19	63.16	76.00	83.33
Treatment group 4, horse serum.....	20	60.00	80.30	91.67
Treatment group 5, blood transfusion.....	12	91.66	63.12	91.67
Treatment group 6, B. perfringens antitoxin and whole blood	12	33.33	67.50	100.00
Treatment group 7, B. perfringens antitoxin and immune serum	12	33.33	96.00	100.00
Treatment group 8, B. perfringens antitoxin and B. coli serum.....	12	33.33	72.00	100.00
Treatment group 9, immune blood serum, lyophilized	12	25.00	48.00	100.00
Combined Mortality of All Treatment Groups except 3, 4 and 5				
Number of Dogs	Lived	Died	Mortality, Percentage	
107	72	35	33.64	

instances showed that the lowered mortality in the treatment group was due to a greater tendency to localization of the process. This is corroborated not only by the lower mortality (74.16 per cent as compared to 39.59 per cent in the control group) but also by the increase in the average number of hours of survival of dogs that died after the operation (nineteen hours, an increase of 29.02 per cent) (table 6).

At subsequent operations on the dogs that recovered the gross findings showed that in the control group the appendix was completely absorbed in 60 per cent of instances and partially absorbed in 40 per cent. In the treatment group, 23 of the dogs were still living when this report was made, and with 8 others notations were not made at the time of the operation.

SUMMARY OF THE TREATMENT OF LAXATIVE-INDUCED
SPREADING PERITONITIS IN DOGS

The mortality from laxative-induced spreading peritonitis in non-treated control groups A, B, and C was 74.16 per cent.

The mortality from laxative-induced spreading peritonitis in dogs treated with horse serum given intramuscularly was 60 per cent.

The mortality from laxative-induced spreading peritonitis in dogs treated with *B. perfringens* antitoxin alone was 41.03 per cent.

The mortality from laxative-induced spreading peritonitis in dogs treated with *B. perfringens* antitoxin given intravenously was 63.16 per cent.

TABLE 7.—*Comparison Between the Control and Treatment Groups*

	Number of Dogs	Average Weight, Kg.	Average Weight, Kg.		Average Dose Castor Oil, Cc.	Treatment			
			Lived	Died					
Control groups.....	89	9.73	9.27	9.90	33.26				
Treatment— B. perfringens antitoxin alone and combined with whole blood, Bacillus coli serum, and immune blood serum	114	9.95	10.88	10.28	24.38	B. Perfringens Antitoxin			
						Average Dose, Cc.	Lived	Died	
						36.1	37.4	34.02	
	Number		Mort- ality, Per- centage	Pathologic Picture		Average Duration of Life of Dogs That Died, Hr.	Subsequent Examination at Operation		Autopsy
	Lived	Died		S. P.	L. P.		A. A.*	L. P.	
Control groups	23	66	74.1	93.9	6.07	65.92	60.0	40.0	5
Treatment—B. per- fringens antitoxin alone and combined with whole blood, Bacillus coli serum, and immune blood serum	70	44	38.5	72.7	18.9	85.02	60.9	39.1	0

* Acute appendicitis.

The mortality from laxative-induced spreading peritonitis in dogs treated with *B. perfringens* antitoxin given intramuscularly was 33.68 per cent.

The mortality from laxative-induced spreading peritonitis in dogs treated with blood transfusions alone was 91.66 per cent.

The mortality from laxative-induced spreading peritonitis in dogs treated with blood transfusion and *B. perfringens* antitoxin given intramuscularly was 33.33 per cent.

The mortality from laxative-induced spreading peritonitis in dogs treated with immune blood serum and *B. perfringens* antitoxin was 33.33 per cent.

The mortality from laxative-induced spreading peritonitis in dogs treated with *B. perfringens* antitoxin combined with polyvalent *B. coli* antitoxin was 33.33 per cent.

The mortality from laxative-induced spreading peritonitis in dogs treated with lyophilized immune serum alone was 25 per cent.

The maximum mortality in the control groups was in control group C—91.87 per cent.

The maximum mortality in the treatment groups was in treatment group 5—91.66 per cent.

The minimum mortality in the groups treated with *B. perfringens* antitoxin was in treatment group 3—26.68 per cent.

The minimum mortality in all treatment groups was in treatment group 9—25 per cent.

The average postoperative duration of life of the dogs that died in the control group was sixty-six hours.

The average postoperative duration of life of the dogs that died in the treatment group was eighty-five hours.

The maximum postoperative duration of life of the dogs that died in the control groups was in group A—sixty-eight hours.

The maximum postoperative duration of life of the dogs that died in the treatment groups was in group 3—one hundred and eighteen hours.

The minimum postoperative duration of life of the dogs that died in the control groups was in group B—sixty-two hours.

The minimum postoperative duration of life of the dogs that died in the treatment groups was in group 9—forty-eight hours.

The average percentage of animals dying from spreading peritonitis, in control groups A, B and C was 94 per cent.

The average percentage of animals dying from spreading peritonitis, in treatment groups 1, 2 and 3, which were treated with *B. perfringens* antitoxin alone, was 50 per cent.

DEGENERATION OF INFUNDIBULAR NERVE FIBERS IN THE CAT WITHOUT APPRECIABLE POLYDIPSIA

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The denervation theory of the causation of diabetes insipidus holds high interest at the present time. This theory is based on the assumption that diabetes insipidus is due to the absence of, or to a deficiency in, the antidiuretic principle which is elaborated by hypophyseal tissue. It depicts that this tissue is activated only by neurogenic influences carried by the nerve fibers which take origin in the hypothalamus and pass to the hypophysis by way of the infundibular stalk.

In an early statement of the theory, the antidiuretic principle was assumed to be elaborated by the epithelial investment of the pars nervosa, namely, by both the pars intermedia and the pars tuberalis.¹ Later, attention was focused on the infundibular process (the enlarged distal portion of the pars nervosa) as the secretory structure. This shift was largely due to the successful extraction of the antidiuretic principle from the neural lobes of birds and whales, which are free from any epithelial investment,² and also to the recognition of anatomic changes in the infundibular process in the cat following hypothalamic lesions which, in turn, were associated with diabetes insipidus.³ The successful occlusion of the hypophyseal stalk in the monkey without elicitation of diabetes insipidus⁴ resulted in the focusing of attention

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1. Cushing, H.: *Papers Relating to the Pituitary Body, Hypothalamus and the Parasympathetic Nervous System*, Springfield, Ill., Charles C. Thomas, Publisher, 1932, p. 31.

2. Geiling, E. M. K.: *Bull. Johns Hopkins Hosp.* **57**:123, 1935.

3. (a) Fisher, C.; Ingram, W. R.; Hare, W. K., and Ranson, S. W.: *Anat. Rec.* **63**:29, 1935. (b) Fisher, C.; Ingram, W. R., and Ranson, S. W.: *The Relation of the Hypothalamico-Hypophyseal System to Diabetes Insipidus*, *Arch. Neurol. & Psychiat.* **34**:124 (July) 1935. (c) Fisher, C., and Ingram, W. R.: *Endocrinology* **20**:762, 1936.

4. Mahoney, W., and Sheehan, D.: *Brain* **59**:61, 1936.

on the entire pars nervosa⁵ as the source of the antidiuretic principle; i. e., the infundibulum as well as the infundibular process.

Except for this change in the hypophysial structure suspected as the secretory tissue, the fundamental denervation hypothesis has remained unchanged—namely, that the elaboration of the antidiuretic principle is dependent on intact hypothalamic innervation. If this is true, complete degeneration of the infundibular nerve fibers should invariably result in the appearance of diabetes insipidus in its maximal form, because the antidiuretic principle would be completely lacking. One would expect the magnitude of the polydipsia per kilogram of body weight to be fairly consistent in a given species and probably from one species to another. Further, in the instance of nearly complete denervation there should be some correlation between the degree of denervation and the severity of the diabetes insipidus.

Several experimental studies are now on record which establish the fact that lesions occurring in the ventral hypothalamus frequently precipitate diabetes insipidus.⁶ Most of the experiments in these series have not been sufficiently controlled anatomically for any attempt at a positive correlation between the occurrence or severity of diabetes insipidus and the extent of degeneration of the infundibular nerve fibers. Fisher and Ingram and their associates have reported such a correlation in their sizable series of experiments on cats and have interpreted their results as supporting rather conclusively the denervation theory. Analysis of their published data gives one the impression that there was considerable variation in the water intake per kilogram of body weight (body weight was stated only infrequently) present in the preparations which they considered totally denervated (ventral infundibulum only). Certainly the maximum fluid intake per unit of body weight encountered by them in experiments on the cat is far below that on record for experiments on the rat and the dog. Richter reported that certain of his rats drank their own weight of water in twenty-four hours. A water intake of 600 to 900 cc. per kilogram per day is not unusual for the diabetic dog. We have encountered an instance of a water intake of 1,300 cc. per kilogram per day for a dog weighing 5.3 Kg. This was in the presence of a high food intake. Taking into account the range in weight of cats, the maximal water intake encountered by Fisher and Ingram for the cat could not

5. Ingram, W. R., and Fisher, C.: *Anat. Rec.* **66**:271, 1936.

6. (a) Camus, J., and Roussy, G.: *Compt. rend. Soc. de biol.* **83**:764, 1920. (b) Houssay, B. A.; Carulla, J. E., and Romana, L.: *ibid.* **83**:1250, 1920. (c) Bailey, P., and Bremer, F.: *Experimental Diabetes Insipidus*, *Arch. Int. Med.* **28**:773 (Dec.) 1921. (d) Curtis, G. M.: *The Production of Experimental Diabetes Insipidus*, *ibid.* **34**:801 (Dec.) 1924. (e) Richter, C. P.: *Brain* **53**:76, 1930.

have been over 250 or 300 cc. per kilogram of body weight, and in most instances it was considerably less. Fisher⁷ informed me that he feels that the water exchange in the cat is below that in the rat and the dog and that he and his associates did encounter maximal diabetes insipidus for the cat in certain of their animals.⁷

MATERIAL AND METHOD

Cats in good physical condition were used, which in most cases had been conditioned to our cage regimen. Water was continually available to them during a twenty-three hour period daily. Food, which consisted of a mixture of half a prepared dog food and half salmon, was available in their cages for sixteen hours daily. The water drunk and the food eaten were measured every twenty-four hours. In some cases during the immediate postoperative period limited milk was given. In these instances the milk was included in graphing fluid intake. In graphing fluid and food intake on the basis of kilogram of body weight, the weight of the animal at operation was used throughout for the basis of calculation. No routine quantitative urinary studies were made. The absence of polydipsia is an adequate criterion for the absence of diabetes insipidus. In addition, we are convinced on the basis of observations in our laboratory that the severity of diabetes insipidus is most reliably measured by the magnitude of the polydipsia.

Operative Procedure.—The ventral portion of the hypothalamus was exposed on one side by the usual intracranial subtemporal approach. Then by means of subpial manipulation in the ventral hypothalamus with a small, blunt probe, an attempt was made to isolate the entire hypophysis from the hypothalamus, thus sectioning the nerve fibers before their entrance into the infundibulum. The whole procedure is easily accomplished with good visibility and with complete hemostasis. The greatest difficulty encountered was in sectioning those fibers which leave the hypothalamus and enter the infundibulum at its anterior extremity. We have now learned to do this with certainty by running the probe anteriorly between the pia and the surface of the hypothalamus and making the lesion by inward traction into the hypothalamus rather than by our former method of outward traction after protruding the probe into the hypothalamic tissue at the level of the infundibulum.

HISTOLOGIC STRUCTURE

The location and extent of the lesion as well as the extent of degeneration of the infundibular nerve fibers were determined at the termination of the experiment by sectioning the hypothalamus-hypophysis block (fixation in solution of formaldehyde and embedding in paraffin) longitudinally and mounting three sets of consecutive sections (every tenth or fifth section). One set was stained for cells with cresyl violet, another for nerve fibers by a modification of the Pal-Weigert method, and the third for nerve fibers by the method of Bodian.⁸ Complete demarcation of the hypophysis from the hypothalamus by scar tissue, as illustrated in figure 1, is sufficient evidence of complete degeneration of the infundibular nerve fibers. Nevertheless, the silver preparations, as illustrated in figure 2, were indispensable in doubtful instances of complete isolation.

We found that the Bodian method was not only reliable but admirable for this study, because of the fact that the cellular elements show up so well

7. Fisher, C.: Personal communication to the authors.

8. Bodian, D.: *Anat. Rec.* 65:1, 1936.

in relation to the nerve fibers. Figure 3 is a low power photomicrograph of a section of the hypophysis and ventral hypothalamus of the cat, stained by this method. Note that at this low power the distal half of the infundibulum shows as a compact nerve trunk; this appearance is produced by a concentration of the nerve fibers in this region. In addition, the various parts of the hypophysis as well as their lines of separation are readily identified. The condensation of the nerve fibers in the distal half of the infundibulum is no doubt due to the progressive decrease in the width and diameter of the infundibulum in going distally from the hypothalamus. This region of concentration of fibers in the infundibulum was therefore particularly scrutinized for nerve fibers in our serial preparations. It is this region of the ventral portion of the infundibulum that is illustrated in the high power photomicrographs in figure 2.

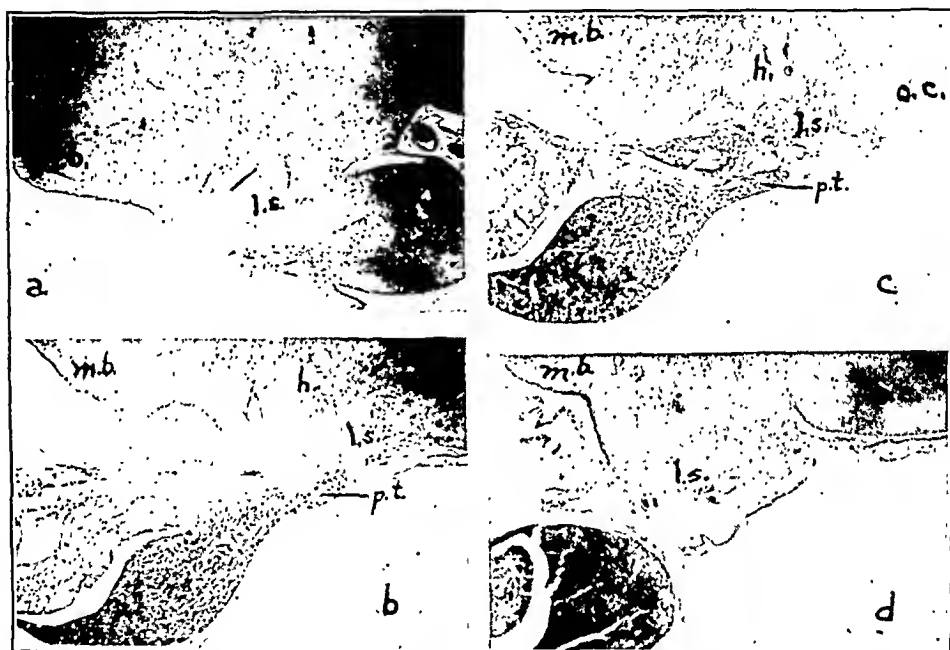


Fig. 1.—Low power photomicrographs of representative sections taken from the serial sections for cat 1, showing the location and extent of the hypothalamic lesion. Sections *a*, *b* and *d* were stained by the Bodian method; section *c* was stained with phosphotungstic acid. Sections *a* and *b* are sections to the left of the midline, and sections *d* and *c*, to the right. The abbreviations are: *m.b.*, mamillary body; *o.c.*, optic chiasm; *l.s.*, lesion scar; *h.*, hypothalamus; *p.t.*, pars tuberalis.

The presence or absence of nerve fibers as well as the general size and number of cellular elements in the infundibular process is likewise somewhat indicative of the extent of degeneration of the infundibular nerve fibers. This fact is illustrated in figure 2

RESULTS

We operated on 29 cats, of which 7 either did not survive the operation long enough for adequate observation or were found dead at such a time that reliable anatomic studies could not be made. The daily food and water consumption of the remaining 22 cats was

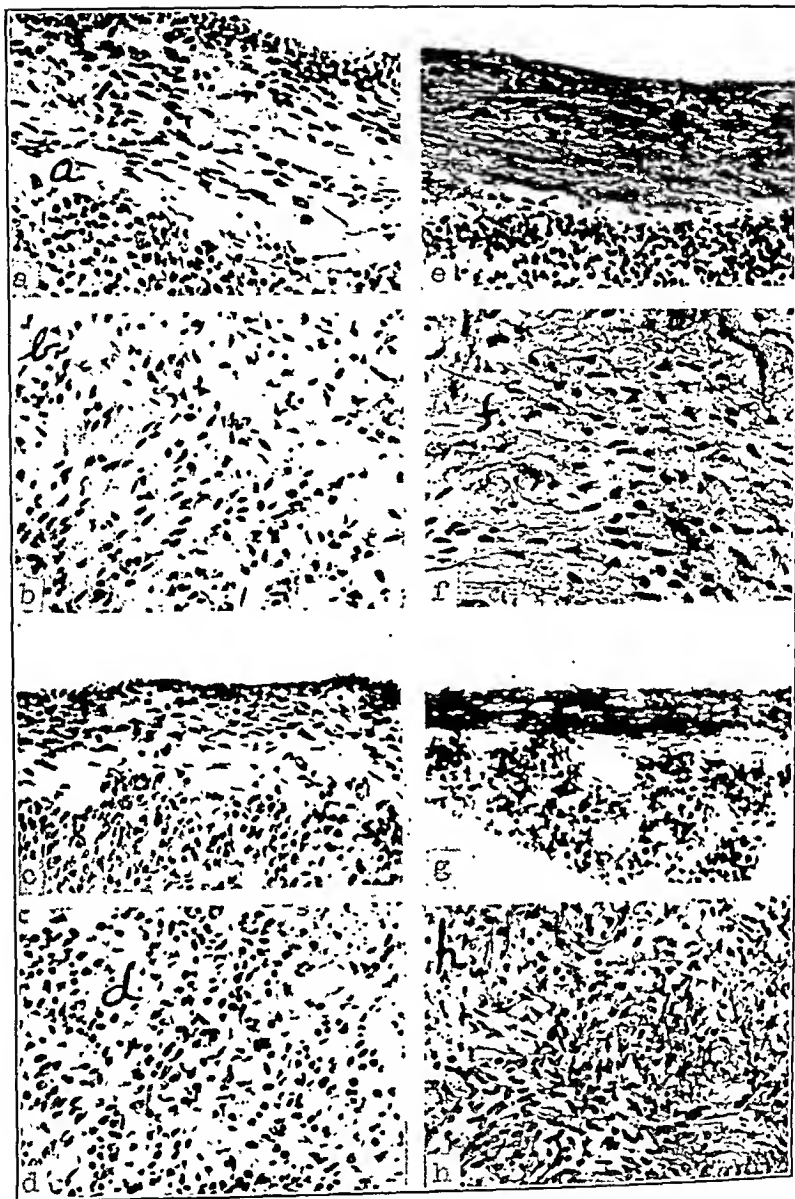


Fig. 2.—Representative high power photomicrographs, all of the same magnification, from sections stained by the Bodian method. Section *a* was taken from the distal region of the ventral infundibulum of cat 2 (as indicated by arrow 1 in figure 3). Compare with *c*, *e* and *g*. Note the absence of nerve fibers, the prominence of cellular elements and the absence of narrowing in the infundibulum. Section *b* was taken from the ventral and somewhat peripheral region of the infundibular process of cat 2 (as indicated by arrow 2 in figure 3). Compare with *d*, *f* and *h*. Note the absence of nerve fibers and the increased number of cellular elements as compared with the normal, shown in *f*. Section *c* (cat 3) is equivalent to sections *a*, *e* and *g*. Note that the width of the infundibulum is less and the cellularity greater than in *a*. Section *d* (cat 3) is equivalent to sections *b*, *f* and *h*. Section *e* was taken from the region of the ventral infundibulum of a normal cat (indicated by arrow 1 in figure 3). Note that the histologic picture of the entire width of the infundibulum at this point is essentially that of a compact nerve trunk. Section *f* was taken from the region of the infundibular process of a normal cat (indicated by arrow 2 and shown in figure 3). Section *g* (cat 4) is equivalent to sections *a*, *c* and *e*. Note that the infundibulum is much narrowed in spite of the presence of many nerve fibers. Section *h* (cat 4) is equivalent to sections *b*, *d* and *f*. Note the increased cellularity as compared with *f*, in spite of the presence of many nerve fibers.

observed over periods ranging from five weeks to five months. During the period of observation the cats remained in good health and exhibited no deviation from the normal in behavior except (for a few days) slight sluggishness and caution in using the jaws because of the soreness of the severed temporal muscle. As a rule their appetites continued normal or slightly enhanced directly after the operation, but in a few instances forced feeding (milk by stomach tube) was necessary for several days, after which spontaneous feeding was resumed. In no instance was there any indication of depressed function of the pars anterior as evidenced by hypoglycemic crises.

In most cases the experiments were terminated at the close of the period of observation of food and water consumption. After the

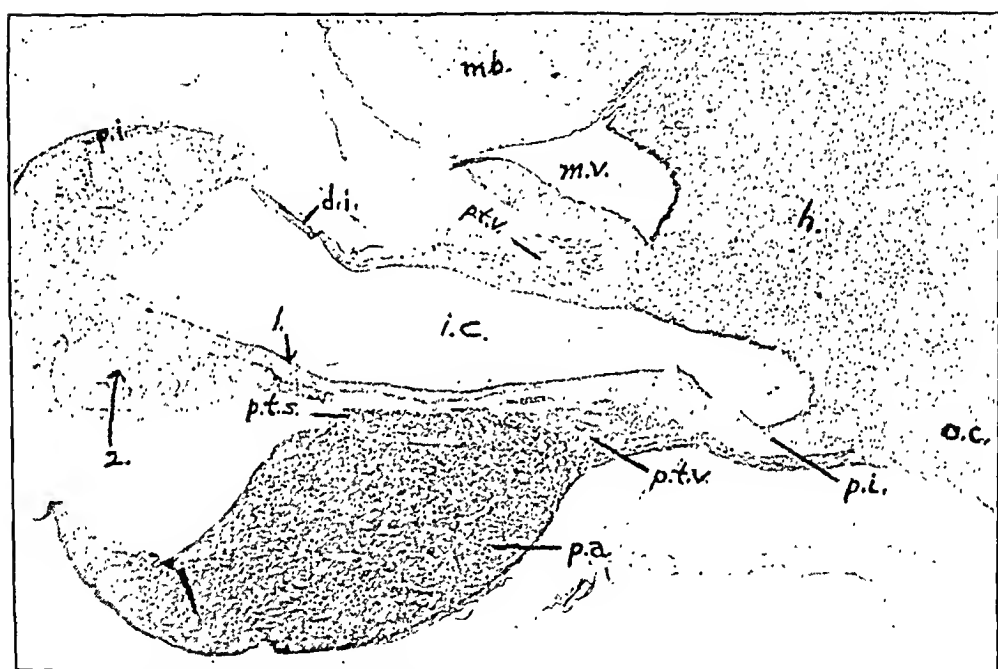


Fig. 3.—Low power photomicrograph of a longitudinal section through the hypothalamus and hypophysis stained by the Bodian method. The abbreviations are: *m.b.*, mamillary body; *h.*, hypothalamus; *o.c.*, optic chiasm; *iii v.*, third ventricle; *i.c.*, infundibular cavity; *pi.*, proximal portion of the infundibulum; *p.t.v.*, pars tuberalis, vascular portion; *p.t.s.*, pars tuberalis solid portion; *p.a.*, pars anterior; *d.i.*, distal portion of the infundibulum. The letters *p.i.*, indicating the infundibular process, are incorrectly placed, but arrow 2 identifies this structure. Arrow 1 indicates the area shown magnified in figure 2 (e); arrow 2 indicates area shown magnified in figure 2 (f).

regimen of cage observation, one group of animals was placed in an outdoor breeding pen in connection with observations on reproduction (summer 1936). These animals became heavily infested with fleas,

and several deaths occurred before the cause of death was ascertained. The cats of this group included in the following report were found either in a state of collapse or shortly after death, so that adequate fixation of the brain tissue was obtained.

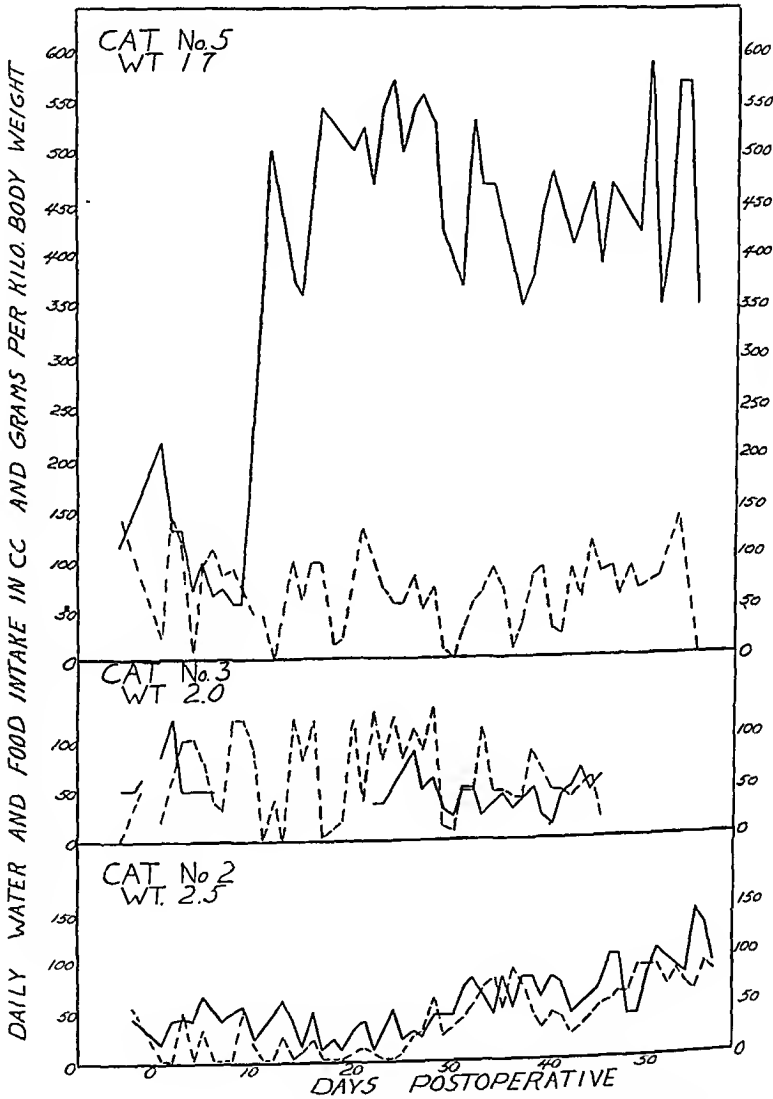


Fig. 4.—Food intake in grams and water intake in cubic centimeters.

Complete degeneration of the infundibular nerve fibers occurred in 9 of the 22 animals. The tissues of 3 of these preparations are illustrated in figures 1 and 2. Only 1 of these 9 animals had striking polydipsia; for 2 others there was a slight elevation in water consumption. The water consumption was normal or essentially so for the remaining 6 animals. The hypophysis was practically denervated in 7

additional animals, since only occasional nerve fibers remained in the pars nervosa. In some of the cases nerve fibers were present only in the posterior portion of the infundibulum, the anterior portion being devoid of fibers. Three of these 7 animals exhibited slight polydipsia, whereas the water consumption was normal or essentially so for the remaining 4. Severance of the infundibular nerve fibers was incomplete in the remaining 6 animals in the group of 22. A large number of nerve fibers were present throughout the extent of the pars nervosa. One of these animals exhibited a slightly enhanced water intake, whereas the others showed no deviation from the normal. The following description is typical of the series.

The daily food and water consumption of the only animal (cat 5) which exhibited striking polydipsia is graphed at the top of figure 4. Note the typical abrupt onset of the permanent phase of the polydipsia during which the water intake ranged from 350 to 575 cc. per kilogram of body weight per day. There was an accompanying polyuria of the same magnitude. The food consumption was normal or slightly enhanced. Subsequent to the period graphed, fifty-fourth day, this cat was placed outside in the breeding yard until the eightieth day, at which time it was again placed on record for a week's period. At this time the water intake remained consistently just above 300 cc. per kilogram of body weight per day. The cat was then returned to the breeding pen and was found in a state of collapse on the one hundred and second day after operation. At the time of operation the cat was in good physical condition, though tending to be lean. It weighed 1.7 Kg. at that time. Just previous to death it weighed 2.2 Kg. Much intra-abdominal fat was noted at autopsy. Good silver preparations were not obtained because of poor fixation and because the hypophysis had been largely separated from the hypothalamus in removal of the brain. The hypophysis had been completely isolated at the time of operation, because the Nissl and Weigert preparations revealed that the hypothalamic tissue below the fornix and caudal to the optic chiasm was involved by the lesion. There was no apparent macroscopic encroachment on the epithelial portion of the hypophysis.

The food and water consumption of cat 3 is graphed immediately beneath that of cat 5 in figure 4. Note that this cat's water consumption did not exceed the preoperative intake in spite of a definitely enhanced food intake. The water intake for a period following operation was not obtained because it was daily contaminated with urine and feces. This cat, as is evident from the record of food consumption, remained in good health throughout the period of observation and exhibited no deviation from the normal in behavior either immediately after operation or subsequently. It weighed 2 Kg. at the time of operation and 2.2 Kg. when killed. It was killed on the forty-ninth day after operation. The

entire ventral tip of the hypothalamus was involved by scar tissue. In addition, the needle path reached at the level of the caudal extent of the optic chiasm dorsally and anteriorly well above the dorsal level of the chiasm. There was some narrowing of the infundibular tissue as well as some central disappearance of the tissue of the infundibular process, so that the infundibular cavity extended slightly into this structure. There was a decided increase in number as well as a decrease in size of the cellular elements of both the infundibular process and the infundibulum. The whole of the pars nervosa was devoid of nerve fibers. Most of these features are readily appreciated in a comparison of the photographs of portions of the infundibulum and infundibular process shown in *c* and *d* in figure 2 with like photographs taken of normal tissue and shown in *e* and *f* in figure 2.

The food and water intake of cat 2 is graphed at the bottom of figure 4. This cat during the first three weeks after operation had a sluggish appetite, although it exhibited normal behavior in other respects. As the food consumption returned to normal or slightly above normal, the water consumption likewise rose above the pre-operative level. This cat, therefore, exhibited a suspected trace of diabetes insipidus, although this is not at all certain in the presence of the high food intake. At the time of operation it weighed 2.5 Kg. During the time of sluggish appetite the weight dropped to 2 Kg. This loss was regained by the time the cat was killed, the sixtieth day after operation. The lesion involved only the extreme ventral portion of the hypothalamus; however, the hypophysis was entirely separated, as the whole of the pars nervosa was devoid of nerve fibers. The tissue of the infundibulum was not narrowed as in cat 4, but there was some central disappearance of the infundibular process. The whole of the pars nervosa exhibited an increase in the number and a decrease in the size of the cellular elements. Most of these features are illustrated in figure 2.

The location and extent of the lesion in cat 1 are illustrated in figure 1. It is readily evident that the hypophysis was entirely isolated from the hypothalamus by scar tissue involving the ventral portion of the hypothalamus. Note also that the lesion involved the hypothalamic tissue just posterior to the optic chiasm, so that it is certain that all fibers coming from the anterior hypothalamus were cut. The rather marked central disappearance of the tissue of the infundibular process is evident in a comparison of this structure, shown in *b* of figure 1, with that of the normal infundibular process, shown in figure 3. At the same time it is seen at this low power that there was no narrowing of the infundibular tissue. The fact that there was no macroscopic infringement on the pars anterior and only slight encroachment on the pars tuberalis is particularly illustrated in *c* of figure 1. This section

is stained with phosphotungstic acid, whereas sections *a*, *b* and *d* are stained by the Bodian method. This cat at operation weighed 1.6 Kg. and eighty-three days later weighed 1.85 Kg., having lost weight immediately after operation. In this instance, food and water consumption was recorded only periodically after the eighteenth day after operation. The average food and water intakes per kilogram of body weight were:

Third week after operation—food 55 Gm.; water 115 cc.

Sixth week after operation—food 115 Gm.; water 120 cc.

Tenth week after operation—food 125 Gm.; water 150 cc.

The graphed curves, therefore, were essentially the same as those for cat 2. It was listed in the statistical grouping as displaying slight polydipsia. The cat was in good health when last weighed, on the eighty-third day after operation, and was found dead on the eighty-eighth day after operation. A fair injection was obtained, so that the location and extent of the lesion as evident from figure 1 were determined adequately.

COMMENT

It is immediately apparent that in this series of experiments there was no correlation between the occurrence or the severity of polydipsia and the extent of degeneration of the infundibular nerve fibers. It is therefore doubtful that the polydipsia which follows certain hypothalamic lesions is primarily the result of sectioning either the whole or any part of the hypothalamicohypophysial system of nerve fibers. If the secretion of the antidiuretic principle were dependent on the intactness of these nerve fibers, we should have encountered a striking and consistent polydipsia (maximal for the cat) in each of the 9 animals in which they were completely degenerated. At the same time, the 7 animals in which essentially all of these fibers were eliminated should have exhibited a polydipsia somewhat near the maximal. The results obtained were in contrast to such an expectancy. A striking polydipsia was encountered with 1 animal only, namely, cat 5. In the other animals in which there was an increase or a suspected increase in water consumption, this increase was so slight as compared with that present in cat 5 that for purposes of analysis they all can be grouped with the animals in which no postoperative increase occurred.

The absence of polydipsia following degeneration of the infundibular nerve fibers in one instance alone is a positive demonstration of the fallacy of the denervation theory, provided the elaboration of the antidiuretic principle is confined to hypophysial structures and that no complicating factors entered into the experiment. We see one possible way in which these experiments may have been complicated; namely, we may have eliminated by our operative procedure the secretion of the

antidiuretic principle and, in addition, paralyzed the mechanism of the pars anterior which is essential for the occurrence of diabetes insipidus in its maximal form. There are several investigations which suggest that the pars anterior mediates its effect in this respect by way of its thyrotropic principle.⁹ The thyroid glands of these animals appeared normal grossly but were unfortunately accidentally discarded before histologic studies were obtained. There was no outward evidence of hypothyroid function and no indication of depressed function of the pars anterior as evidenced by hypoglycemic crises. There was in no instance any macroscopic evidence of involvement of the pars anterior of the hypophysis. Nevertheless, the possibility of such a complication must be ruled out in another series of experiments designed to answer the question.¹⁰

It should be pointed out that, assuming that these experiments were not complicated as has been outlined, they do not necessarily eliminate the possibility that the pars nervosa may be a structure which elaborates the antidiuretic principle. There were healthy-looking cellular elements in the remaining tissue of the pars nervosa, which on the basis of their histologic structure might be suspected of a secretory function as readily as might the cellular elements in the normally innervated pars nervosa. Although there was a decided increase in the cellular elements of the pars nervosa following degeneration of the infundibular nerve fibers, the staining characteristics of the cells were not changed, as evidenced by cresyl violet preparations. This is illustrated in figure 3 of a previous paper.^{10a} Again, the denervation concept might hold with reference to the pars nervosa if, perchance, the tissue of the hypothalamus possesses, in common with the pars nervosa, antidiuretic secretory powers.¹¹ We

9. (a) Barnes, B. O.; Regan, J. F., and Bueno, J. G.: *Am. J. Physiol.* **105**:559, 1933. (b) Biasotti, A.: *Compt. rend. Soc. de biol.* **115**:329, 1934. (c) Mahoney, W., and Sheehan, D.: *Am. J. Physiol.* **112**:250, 1933. (d) Keller, A. D.: *Proc. Soc. Exper. Biol. & Med.* **36**:787, 1937.

10. Since this paper was submitted for publication (December 1937) it has become clear that impairment of function of the anterior lobe would not materially complicate such experiments because, contrary to one school of thought,⁵ a functioning pars anterior is not essential for the occurrence of permanent moderate diabetes insipidus (Keller, A. D.: *Proc. Soc. Exper. Biol. & Med.* **38**:31, 1938; *Am. J. Physiol.* **123**:111, 1938. White, H. L., and Heinbecker, P.: *ibid.* **123**:213, 1938). This fact was shown particularly well in a series of experiments on 8 dogs, in which we made certain of total hypophysectomy by deliberate infringement on the ventral portion of the hypothalamus. The animals, with a constant food intake, without exception showed permanent polydipsia, drinking from 200 to 300 cc. of water per kilogram of body weight per day. All experiments were continued six months or longer. Complete removal of the pars anterior was evident because (1) sensitivity to insulin was increased twenty times or more, (2) removal of the pancreas resulted in no appreciable diabetes mellitus, (3) basal metabolism was lowered appreciably, and (4) thyroid and adrenal glands showed marked atrophy.

feel on the basis of our own experience with the cat and the dog that the more traumatic the lesion in the hypothalamus the greater is the likelihood that diabetes insipidus will follow. Thus the incidence of severity and permanence of diabetes insipidus following lesions in the ventral hypothalamus, designed to sever all infundibular nerve fibers, is greater for the dog than for the cat. This may well be due to the much greater active vascularization of the hypothalamic region in the dog, which enhances the destructiveness of the lesions.

With reference to the changes encountered in the pars nervosa, the extent of central disappearance of the infundibular process as well as the thinning of the infundibulum was variable and could not be correlated with the extent of the degeneration of the infundibular nerve fibers. This fact is amply demonstrated with reference to the infundibulum in figure 2. Thus, in cat 4 the infundibulum was considerably thinned even though all the nerve fibers were not degenerated. In cats 2 and 3 all the nerve fibers were degenerated; the infundibulum was not encroached on in cat 2 but was markedly narrowed in cat 3. Therefore, the central disappearance of the tissue of the pars nervosa bordering on the infundibular cavity was due to some factor other than the degeneration of the infundibular nerve fibers. We are now certain that this is true of the dog also, because we have succeeded in degenerating all the infundibular nerve fibers, both by a lesion in the ventral hypothalamus and by section of the stalk, without any central disappearance of the tissue of the infundibular process. The increased cellularity, on the other hand, would seem to be in part the direct result of degeneration of the nerve fibers and probably is due to a phenomenon similar to the cellular proliferation which follows any degeneration within the central nervous system.

On the basis of comparative data for the rat and the dog, it is doubtful that the maximum severity of diabetes insipidus for the cat was encountered with cat 5. It seems certain that the polydipsia of this cat was far greater than the maximum encountered by Fisher and Ingram. This may have been merely the reflection of a larger food consumption with a higher salt content than that of the cats in the Chicago series. However, this factor alone hardly seems sufficient to explain this difference in magnitude of the polydipsia encountered.

SUMMARY

The hypophysis was isolated from its entire direct hypothalamic nerve supply in several cats without eliciting any appreciable polydipsia.

10a. Keller, A. D.; Noble, W., and Hamilton, J. W., Jr.: *Am. J. Physiol.* **117**:467, 1936.

11. Keller, A. D.; Noble, W., and Hamilton, J. W., Jr.: *Proc. Soc. Exper. Biol. & Med.* **34**:794, 1936.

SERUM THERAPY FOR INFECTIONS WITH STREPTOCOCCI

GENERAL OBSERVATIONS

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AND

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In an earlier series of four papers we presented a brief account of our experience up to October 1933 in the treatment of infections due to hemolytic streptococci by use of the concentrated antistreptococcus serum of the New York state department of health. Our results at that time indicated a favorable effect of the serum, although the observations were not regarded as conclusive. We quote a paragraph from the first of these papers:¹

In some diseases the natural course of the malady, when uninfluenced by therapeutic meddling, tends to follow a more or less definite schedule and to terminate in recovery or in death. In other disorders the course tends to be variable, and the complications and the eventual outcome are lacking in uniformity. Infections with the hemolytic streptococci belong in the latter category. On that account the appraisal of any therapeutic agent for streptococcic infections is made difficult, and any decisive statement in regard to this matter is calculated to promote controversy rather than conviction.

Certainly more light is needed. The recognition of different serologic types of hemolytic streptococci by Griffith² warrants the hope for further improvement in the therapeutic efficiency of serums for infection by these organisms. Evidence indicating the positive value of serum at present available may be expected to encourage further attempts to prepare more potent serum. The use of such serum in conjunction with other therapeutic agents, such as the sulfonamides and

From the Department of Pathology and Bacteriology, New York Post-Graduate Medical School and Hospital, Columbia University.

1. Sheplar, A. E.; Spence, M. J., and MacNeal, W. J.: *Therapeutic Use of Concentrated Anti-Streptococcus Serum of the New York State Department of Health*, Arch. Surg. **29**:858-865 (Nov.); 1065-1075 (Dec.) 1934; **30**:1-13 (Jan.); 357-370 (Feb.) 1935.

2. Griffith, F.: *Serological Classification of Streptococcus Pyogenes*, J. Hyg. **34**:542-584 (Dec.) 1934.

the bacteriophages, challenges investigation. The untoward effects of injections of serum also require further elucidation. Some attention will be given to these questions in the present consideration of our additional cases in which streptococcus serum therapy has been employed since 1933.

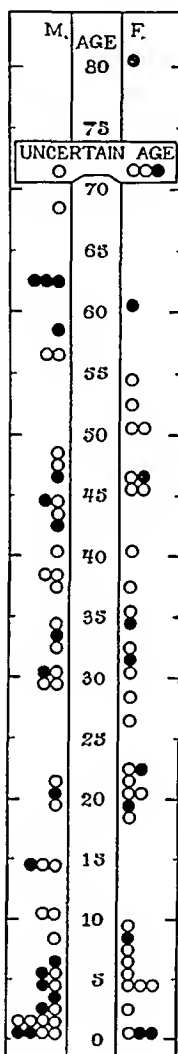


Chart 1.—Distribution according to age and sex of 92 patients treated with streptococcus serum. The hollow circles indicate survivals, and the solid black circles indicate deaths.

The entire series of cases will be presented. It is easy to pick out for exhibition a few startling examples of success and to conceal the failures, thus giving support to the pretense that some particular method of treatment yields miraculous results. We wish not to do this. It is, however, only fair to say that the patients in our series have come

Data on Sixty-Six Patients

No.	Date	Patient	Sex	Age	Condition at Onset	Operations
1933						
27	Oct. 16	T. B. H.	M	29	Compound fracture	Oct. 4, Oct. 17
28	Oct. 28	M. F.	F	46	Fracture of right leg; pharyngitis	Nov. 10, Nov. 14, Dec. 8
29	Oct. 31	R. C.	M	14	Mastoiditis	Oct. 31, Nov. 29
30	Nov. 22	S. T.	F	9	Rheumatic fever	None
31	Dec. 7	F. C.	M	Adult	Cellulitis of finger	None
32	Dec. 20	H. H.	F	2½	Cellulitis of right arm	Dec. 20
1934						
33	Jan. 14	B. F.	M	5	Meningitis	Jan. 13
34	Jan. 17	C. F.	M	15½	Recurrent otitis media	Previous
35	Jan. 25	A. F.	M	10	Cellulitis of leg	Jan. 23, Mar. 5
36	Jan. 26	P. W.	M	37	Postoperative infection	Jan. 22
37	Feb. 14	K. B.	F	7	Mastoiditis	Feb. 13, Mar. 15
38	Mar. 3	W. R. B.	F	30	Ulcers of leg	None
39	Apr. 7	J. M.	M	10	Meningitis	Apr. 1, Apr. 7
40	Apr. 16	J. D.	M	44	Cellulitis of leg	Apr. 12, 24, May 2
41	Apr. 18	N. M.	F	Child	Meningitis	Apr. 10
42	June 6	L. I.	F	4½	Otitis media	June 5
43	July 1	P. F.	F	8	Peritonitis	June 25
44	July 25	D. M.	F	35	Cellulitis of right leg	July 27
45	July 30	E. O.	F	31	Puerperal sepsis	July 16
46	Aug. 18	L. R.	F	22	Puerperal sepsis	None
47	Nov. 29	E. C.	M	30	Mediastinitis drained	Sept. 30, Oct. 15, Nov. 19, 26, Dec. 4, 10
1935						
48	Jan. 8	C. F.	M	14	Osteomyelitis, pericarditis	Jan. 6, 23
49	Jan. 11	J. B.	F	80	Mastoiditis, meningitis	Jan. 6
50	Jan. 12	S. S.	F	52	Cellulitis of hand	Dec. 27, 30, Jan. 9, 13,
51	Jan. 12	J. Z.	M	1	Pneumonia; otitis media	Jan. 10, 12, 16, 23,
						Mar. 28
52	Feb. 15	R. N.	M	62	Mastoiditis; sepsis	Feb. 8, 12
53	Feb. 28	A. C.	F	45	Postoperative	Feb. 24
54	Mar. 2	R. A.	M	11½	Abscess of neck	Feb. 18
55	Mar. 4	M. B.	M	6	Otitis media	Mar. 4
56	Mar. 5	M. L.	M	4	Suppurative knee joint	Mar. 2
57	Apr. 3	W. Y.	M	56	Postoperative	Mar. 11
58	Apr. 10	J. P.	M	11½	Temperature 106 F. Apr. 9	None
59	Apr. 25	E. R.	M	62	Postoperative	Apr. 18
60	Apr. 29	J. G.	F	4½	Otitis media; cervical abscess	Mar. 30, Apr. 26
61	May 1	W. F.	M	5½	Erysipelas	None
62	May 7	E. F.	M	1½	Osteomyelitis	Apr. 22, May 7, 16
63	May 8	R. G.	M	40	Cellulitis of arm	May 10, 18
64	May 11	L. S.	M	5	Otitis media	May 8, 10
65	May 16	C. R.	M	56	Postoperative	Apr. 16
66	May 20	A. P.	F	8½	Peritonitis	May 25
67	June 5	M. M.	F	4	Otitis media; sepsis	May 31, June 1
68	June 9	M. H.	F	50	Diabetes; abscesses	None
69	July 22	W. L.	M	68	Cellulitis of arm	July 15
70	Sept. 14	L. C.	M	21	Osteomyelitis	Previously
1936						
71	Jan. 25	J. J.	F	Adult	Pharyngitis	None
72	Jan. 28	A. C.	M	33	Postoperative meningitis	Jan. 23, 26, 28
73	Feb. 10	D. B.	F	22	Pneumonia; empyema; sepsis	Feb. 9, 10, 11, 18, 21
74	Feb. 21	E. M.	F	50	Perforated esophagus	Feb. 13
75	Mar. 18	H. T.	M	14	Empyema	Mar. 13, 30, 31,
						Apr. 27, 28
76	Mar. 18	T. L.	F	32	Pneumothorax	Feb. 12, 14, 18, 22,
						Mar. 5, 12
77	Mar. 30	S. R.	M	29	Post-operative paratyphoid	Mar. 25, 26, Apr. 4, 8, 22
78	Apr. 3	W. H.	M	43	Post-operative otitis media	Apr. 1, 3, 10
79	Apr. 29	W. B.	M	8	Post-operative pharyngitis	Apr. 17, 27, May 3, 15
80	Mar. 6	A. S.	F	45	Post-operative pharyngitis	Apr. 24
81	May 16	J. N.	M	44	Meningitis and mastoiditis	May 15
82	June 15	B. G.	M	20	Fracture of skull; meningitis	June 11, 14, 22
83	Nov. 2	E. S.	M	38	Chronic colitis	None
84	Nov. 25	X. G.	F	34	Leukemia	Jan. 7, 9
1937						
85	Jan. 14	G. P.	M	32	Sinusitis	Jan. 12
86	Jan. 29	R. W.	F	54	Cellulitis; sepsis	None
87	Feb. 16	V. B.	M	34	Mastoiditis	Feb. 16
88	Feb. 21	E. R.	F	28	Cellulitis of face	None
89	Apr. 18	K. C.	F	40	Cavernous sinus; sepsis	None
90	May 18	B. D.	M	42	Otitis; sepsis; pneumonia; endocarditis (?)	None
91	May 18	P. F.	M	58	Bacterial endocarditis	None
92	July 3	B. S.	F	26	Chronic colitis; rheumatic fever	None

* "N.Y.S. concn." or "N.Y.S. reg." indicates New York state concentrated or regular streptococcus serum; P.D., Parke, Davis & Co. serum, biological 2005.

Treated with Streptococcus Serum

Positive Blood Culture	Time of Serum Therapy	Serum Used*	Comment
Oct. 12, 16, 19, 25	Oct. 16-Dec. 13	N.Y.S. conc. 118,170 units	Recovered
None	Oct. 23-Dec. 27	N.Y.S. conc. 624,000 units	Died Dec. 27
Oct. 28, 30, Nov. 3, 8, 17	Oct. 31-Nov. 16	N.Y.S. conc. 355,400 units	Recovered
None	Nov. 22-Apr. 24	N.Y.S. conc. app. 24,052 units	Lived
None	Dec. 7-Dec. 10	N.Y.S. conc. 7,500 units	Recovered
Dec. 18	Dec. 20-Dec. 22	N.Y.S. conc. 40,000 units	Recovered
None	Jan. 14-Jan. 21	N.Y.S. conc. 460,000 units	Died Jan. 23
None	Jan. 17-Jan. 26	N.Y.S. conc. 18,900 units	Had prompt relief
None	Jan. 25	N.Y.S. conc. 20,000 units	Recovered
None	Jan. 26-27	N.Y.S. conc. 80,000 units	Recovered
Feb. 12, 13, 14	Feb. 14-Feb. 22	N.Y.S. conc. 240,000 units	Recovered
None	Mar. 3-Mar. 8	N.Y.S. conc. 60,000 units	Unimproved
None	Apr. 7-Apr. 12	N.Y.S. conc. 108,000 units	Recovered
Apr. 16	Apr. 16-Apr. 17	N.Y.S. regular 15,000 units	Recovered
None	Apr. 18-Apr. 23	N.Y.S. conc. 440,000 units	Died Apr. 25
June 4, 6, 7, 8, 18, 20	June 6-June 9	N.Y.S. conc. 200,000 units	Recovered
June 26	July 1	N.Y.S. conc. (1.95 cc.) 3,510 units	"Serum death"
July 30	July 25-July 26	N.Y.S. conc. 51,620 units	Recovered
July 23	July 30	N.Y.S. conc. 3,600 units	Recovered
None	Aug. 18	N.Y.S. conc. 60,000 units	Died. Aug. 19
None	Nov. 29	N.Y.S. conc. 40,000 units	Recovered
Jan. 23, 25	Jan. 26	N.Y.S. conc. 60,000 units	Died Jan. 27
None	Jan. 11-Jan. 13	N.Y.S. conc. 38,000 units	Died Jan. 14
None	Jan. 12	N.Y.S. conc. 65,000 units	Recovered
Jan. 11	Jan. 12-13	N.Y.S. conc. 120,000 units	Recovered
Feb. 11, 15, 16	Feb. 15-16	N.Y.S. conc. 100,000 units	Died Feb. 17
None	Feb. 28	N.Y.S. conc. 40,000 units	Recovered
Mar. 1, 3, 4, 5, 7, 9, 13	Mar. 2-Mar. 8	N.Y.S. conc. and reg. 170,000 units	Recovered
Mar. 4, and others	Mar. 4-14	N.Y.S. conc. 140,000 units	Died Apr. 5
None	Mar. 5-6	N.Y.S. conc. 60,000 units	Recovered
None	Apr. 3	N.Y.S. conc. 25,000 units	Recovered
Apr. 10	Apr. 12-13	N.Y.S. conc. 40,000 units	Recovered
None	Apr. 24-25	N.Y.S. reg. 50,000 units	Died Apr. 25
Apr. 27	Apr. 29-May 3	N.Y.S. conc. 100,000 units	Recovered
May 2	May 1 and May 3-May 7	N.Y.S. reg. and conc. 50,000 units	Died May 8
Staph. pos., Strep. neg.	May 7, 1935-Mar. 19, 1936	N.Y.S. conc. 524,200 units and P.D. 17.5 cc.	Recovered
None	May 8-June 4	N.Y.S. conc. 176,000 units	Recovered
May 0	May 11-July 11	N.Y.S. conc. 804,400 units	Recovered
None	May 16, 20, 29, June 2	N.Y.S. reg. 70,000 units	Recovered
May 25	May 26	N.Y.S. conc. 40,000 units	Died May 26
June 2, 16	June 5-June 17	N.Y.S. conc. 150,000 units	Recovered
None	June 9-June 12	N.Y.S. conc. 20,000 units	Recovered
None	July 22-July 31	Eli Lilly	Recovered
None	Sept. 14, 1935, Jan. 24, 1937 and Mar. 6, 1937	P.D. 23.63 cc.	Improved
None	Jan. 25-Jan. 26	P.D. 20 cc.	Recovered promptly
None	Jan. 28-Jan. 30	P.D. 49 cc.	Died Jan. 31
Feb. 10	Feb. 10-Apr. 6	P.D. 760 cc.	Healed
None	Feb. 21-Mar. 3	P.D. 85.6 cc.	Improved
None	Mar. 18-May 31	P.D. 157.85 cc.	Recovered
None	Mar. 18-Mar. 27	P.D. 87 cc.	Recovered
None	Mar. 30-June 30	P.D. 8.242 cc.	Improved
None	Apr. 3-May 19	P.D. 150.71 cc.	Recovered
Apr. 29	Apr. 30-May 18	P.D. 2 cc., N.Y. reg. 91,500 units	Recovered
None	May 6-May 20	P.D. 14.54 cc.	Recovered
None	May 16	P.O. 26 cc.	Died May 17
None	June 15-June 19	P.D. 41.005 cc.	Died June 26
None	Nov. 4-Jan. 23	P.D. 102.2 cc.	Improved
None	Nov. 25-Feb. 2	P.D. 322.9 cc.	Died Feb. 3
None	Jan. 14-Jan. 21	P.D. 13.1 cc.	Recovered
Jan. 28	Jan. 29-Feb. 9	P.D. 18.55 cc.	Cellulitis cured
None	Feb. 16-Feb. 28	P.D. 15.6 cc.	Had rapid healing
None	Feb. 21-Feb. 28	P.D. 26.81 cc.	Recovered
Apr. 16	Apr. 18-May 29	P.D. 238.5 cc.	Recovered
May 7, 8, 22, June 6	May 18-June 13	P.D. 340 cc.	Died June 14
Repeated Str. viridans	May 18-July 4	N.Y.S. conc. 136,980 units	Died July 7
None	July 3-Aug. 7	P.D. 48.7 cc. P.D. 7.33 cc.	Improved

to our attention not in the course of private clinical service but by reference or by request for consultation and, in general, only after the condition had been recognized as desperate. In our earlier report we presented the records of 26 patients. For the present discussion there are data on 66 further patients. The cases are listed in chronologic order, according to the date of institution of serum therapy, in the accompanying table. Various clinical conditions are represented. We purpose to group the cases according to regional specialty and to discuss in more detail each such group in the subsequent papers of this series. In the present paper only the more general features will be discussed.

The age and sex distribution of the entire 92 patients, including the 26 of our previous report and the present 66, is indicated in chart 1. The youngest patient was a boy aged 19 days and the oldest a woman aged 80 years. Evidently there is no exemption from streptococcic infection at any age or in either sex.

In the present group of 66 patients, 18 died and 48 recovered from the streptococcic infection; the death rate, therefore, was 27.3 per cent. Some of the deaths were evidently due to causes not directly related to infection with hemolytic streptococci, while others were due to such infection which was not controlled by treatment. A brief review of each fatality will be undertaken.

REPORT OF CASES

CASE 62.—W. F., a boy aged 5 months, was admitted to the hospital on April 30, 1935, with an infection of the upper respiratory tract, present since April 23. On admission there was purulent rhinitis. There were also swelling of the right lower part of the face and erysipelas of the face, the neck and the upper part of the thorax. On May 1, 10.5 cc. of erysipelas antitoxin (Squibb) was given in divided doses into muscle. On May 2, a culture of the blood was made, which later gave a positive growth of hemolytic streptococci. Another ampule of erysipelas antitoxin was given on this day. On May 3, as the culture of the blood was yielding bacteria, a transfusion of 150 cc. was given and also 10,000 units of the concentrated streptococcus serum of the New York state department of health. The child was exposed to ultraviolet radiation for two minutes. The dose of serum was repeated on May 4. On May 5 a culture of the blood was taken, and this remained sterile; 20,000 units of the same serum was given. On May 6, the culture remaining sterile, the concentrated serum was discontinued, and 5,000 units of unconcentrated streptococcus serum (New York state) was given intravenously. This dose of serum was repeated on May 7, intravenously. The baby died at 2:45 p. m., May 8. Permission for necropsy was not obtained. The clinical diagnosis at the end was pneumonia of the upper lobe of the left lung.

CASE 67.—A. P., a girl aged 8 months, was admitted to the hospital on May 25, 1935, with high fever (temperature 104.6) and a distended, tense abdomen. Laparotomy on this same day disclosed generalized peritonitis without recognizable primary focus. Cultures of the blood and of the peritoneal fluid gave a positive growth of hemolytic streptococci. On May 26, when these cultures had developed, we were asked to see the infant. Concentrated streptococcus serum (New York state), 40,000 units, was given in divided doses, and 30 cc. of stock streptococcus

bacteriophage in asparaginic medium was introduced into the peritoneal cavity along the surgical drain. The patient died at 11:45 p. m., May 26. Necropsy was not permitted.

CASE 33.—B. F., a boy aged 5 years, was admitted to the hospital on Jan. 12, 1934, with otitis media on the left side, a temperature of 104.6, and signs of meningitis. A spinal tap on this day yielded cloudy spinal fluid containing hemolytic streptococci. On January 13 a mastoidectomy was done on the left side. On January 14, treatment with concentrated streptococcus serum (New York state) was started, 20,000 units into the spinal canal and 20,000 units intravenously, and the serum was continued daily through January 21, in increased amount toward the last, to a total of 200,000 units into the spinal canal and 260,000 units intravenously. The patient died January 23 at 3:30 a. m., and necropsy disclosed generalized purulent meningitis and bronchopneumonia of the lower lobe of the right lung.

CASE 56.—M. B., a boy aged 6 years, was admitted to a hospital in Westchester County on Feb. 27, 1935, with otitis media and a temperature of 104 F. Mastoidectomy was performed on March 4. Cultures of the blood made on March 4 and several times thereafter gave a positive growth of hemolytic streptococci. Concentrated streptococcus serum (New York state) was given in the period from March 4 to March 14, a total amount of 140,000 units. Apparently it was then discontinued. Bronchopneumonia and multiple pulmonary abscesses developed. The child died April 5.

CASE 43.—P. F., a girl aged 8, was admitted to the hospital on June 25, 1934. On the next day laparotomy was performed and the appendix was removed. Generalized peritonitis without recognizable focus was present. Hemolytic streptococci were found in culture of the peritoneal fluid and also in culture of the blood. Concentrated streptococcus serum (New York state) was given on July 1, producing fatal anaphylactic shock. (This case will receive more detailed consideration when we come to discuss serious untoward serum reactions and their prevention.)

CASE 41.—N. M., a girl aged about 10 years, was seen by us at Dobbs Ferry, N. Y., on April 18, 1934. Spinal tap at this time yielded a turbid fluid containing hemolytic streptococci. Concentrated streptococcus serum (New York state) was administered into the spinal canal and intravenously. The patient seemed to improve for a time, but we learned subsequently that she died April 25, 1934.

CASE 49.—C. F., a boy aged 14, was admitted to a hospital on Jan. 4, 1935, with osteomyelitis of the right ilium. He had been ill since Dec. 30, 1934. Cultures of blood on January 4 and January 5 gave a positive growth of staphylococci. On January 5 an operation for drainage of the ilium and counterdrainage of the hip was performed, and a transfusion was given. The temperature reached 106. Staphylococcus bacteriophage was administered. On January 23 pericardostomy was performed. A culture of the blood was reported on January 26 as yielding streptococci but not staphylococci. Concentrated streptococcus serum (New York state), 60,000 units, was given on January 26. The patient died January 27.

CASE 82.—B. G., a man aged 20, was injured in an automobile accident May 30, 1936, and was transferred to the New York Post-Graduate Medical School and Hospital on June 10, 1936. On June 11 a bilateral cerebral exploration was performed without discovery of any purulent focus. On June 13 pus was aspirated from an abscess over the sacrum; this pus contained hemolytic streptococci. Bacteriotherapy was requested and initiated on June 15, and streptococcus serum (Parke, Davis & Co., biological 2005) was given daily from June 15 to June 19, the total amount being 41,005 cc. The sacral lesion improved. A sup-

purating laceration of the face contained staphylococci, and on this account staphylococcus bacteriophage was administered on June 23 and 24. The patient died on June 26, and at necropsy, in addition to the external lesions of the face and the sacrum and the surgical wounds of the skull, there was disclosed a fracture of the base of the skull with basilar meningitis apparently extending from a lacerated sphenoid sinus.

CASE 47.—L. R., a woman aged 22, was a private patient whom we did not see. She was delivered of a child at 8:11 p. m. on Aug. 5, 1934. Her temperature remained normal until 8 a. m. on August 8 and then rose, reaching 104.4 F. at 8 p. m. on that day. Cultures of material from the uterine cervix on August 14 yielded a growth of *Streptococcus viridans* and *Staphylococcus albus*. Another culture made from the uterine discharge on August 17 yielded a growth of hemolytic streptococci. No culture of the blood yielding bacteria was ever obtained. Pneumonia was recognized on August 16, and it became progressively more serious. On August 18 concentrated streptococcus serum (New York state) was given in divided doses to a total amount of 60,000 units, without evident effect. The patient died at 12:15 p. m. on August 19.

CASE 72.—A. C., a man aged 33, was admitted to the hospital on Jan. 22, 1936, and on January 23 a laminectomy was performed for neoplasm of the spinal cord. On January 26 the surgical wound was found to be grossly infected, and revision of the wound disclosed an abscess containing 10 to 15 cc. of pus. The cultures yielded hemolytic streptococci. A culture of blood made on January 27 remained sterile. On January 28 further revision of the wound released more purulent collections. Streptococcus serum (Parke, Davis & Co., biological 2005) was given intravenously after the usual series of desensitizing doses, a total amount of 19 cc. on January 28, 10 cc. on January 29 and 10 cc. on January 30. The patient died January 31. Necropsy was not permitted.

CASE 84.—X. G., a woman, aged 34, the wife of a physician, was admitted to a neighboring hospital on Nov. 25, 1936. She had a persistent extensive and deep ulceration of the left side of the mouth and the blood picture of myelogenous leukemia with high grade anemia. The gangrenous ulcer of the mouth contained a mixture of micro-organisms, among which hemolytic streptococci, staphylococci, fusiform bacilli and spirochetes were conspicuous. Along with daily transfusions and chemotherapy with sulfanilamide and neoarsphenamine the patient received staphylococcus bacteriophage and streptococcus serum (Parke, Davis & Co., biological 2005). The total amount of serum used was 323 cc. It was given daily from Nov. 25 to Feb. 2, 1937. The patient died February 3, early in the morning, apparently from meningitis caused by extension of the lesion of the mouth into the left orbit and along the optic nerve. An attempt at surgical drainage of the orbit had been made. Bacteriologic examinations of the slowly progressive lesion indicated the suppression of the streptococci and the staphylococci. For a time there seemed to be relative remission of the leukemia, but the blood picture of leukemia again returned shortly before death.

CASE 90.—B. D., a man aged 42, was admitted to the New York Post-Graduate Medical School and Hospital on May 17, 1937, by transfer from another hospital. Early in April he had pharyngitis, and later, otitis media on the right side and spontaneous rupture of the tympanic membrane. Early in May he had a severe chill, and he entered the first hospital on or about May 6. Repeated cultures of the blood yielded hemolytic streptococci. On May 11 a roentgenologic diagnosis of bilateral mastoiditis was made. The temperature ranged from 99 to 106. Sulfanilamide, 15 grains every three hours by mouth, and prontosil soluble (the disodium salt of 4-sulfamidophenyl-2'-azo-7'-acetyl-amino-1'-hydroxynaphthalene-3',6'-disulfonic acid) 50 cc. every twenty-four hours in divided intramuscular doses

was administered. The patient became cyanotic. On May 13 pneumonia and pleurisy in the right lower quadrant of the thorax were so distressing that this side was taped. The patient was transferred to the New York Post-Graduate Medical School and Hospital May 17, in an unsatisfactory condition, in the hope that serum therapy might be of help. On May 18 a culture of the blood was made, and this remained negative. Methemoglobin was detected by spectroscopic examination of the blood. Cultures of the blood made on May 22 and June 6 yielded bacteria. The painful pleurisy on the right side disappeared, but the physical signs of airless portions of lung persisted. Roentgen study of the thorax revealed patches of infiltration in both lungs but no evidence of pleural effusion. A thoracentesis on the right side was done on June 7, but only 3 cc. of bloody fluid, containing a few flakes of fibrinopurulent membrane, could be obtained. Irregular cardiac action, rapid pulse, low and variable blood pressure and paroxysmal dyspnea, together with the patchy distribution of the pneumonia, led to the strong suspicion of tricuspid vegetative endocarditis. The patient died at 7:20 a. m., June 13. Necropsy was not permitted, so the scientific value of the case is seriously impaired.

Because of the apparently unfavorable progress and the evident methemoglobinemia, the administration of sulfanilamide was interrupted on May 17. Streptococcus serum (Parke, Davis & Co., biological 2005) was given in divided doses on May 18 to a total amount of 25.15 cc. and was continued daily until June 2, the total amount used being 340 cc. for the sixteen days. Subsequently the concentrated serum of the New York state department of health was used, from June 3 to June 13 inclusive, the total amount being 76.1 cc. in eleven days. Sulfanilamide was again given by mouth on May 23 and thereafter; prontosil soluble was injected intravenously, and a specific bacteriophage prepared for the streptococcus yielded by culture of the patient's blood was used intravenously, beginning on June 3. Transfusions were given daily from June 3 to June 13. Various consultants saw this patient during his illness. There were no important differences of opinion.

CASE 81.—J. N., a man aged 44, was admitted to the hospital April 28, 1936, with chronic inflammation of the paranasal sinuses, acute pharyngitis and an abscess along the lower jaw. On May 6 the abscess was incised. On May 15 the patient had a chill lasting thirty minutes and became stuporous. A culture of the blood, made at this time, remained sterile. Spinal tap yielded cloudy fluid showing pus cells and streptococci in the direct microscopic examination and, on culture, hemolytic streptococci. At 12 midnight a simple mastoidectomy was performed, and cultures of material from the mastoid also showed streptococci. On May 16 serum therapy was requested, and multiple doses to a total amount of 26 cc. were given from 12:38 to 3:48 p. m. The patient then went into a chill lasting thirty minutes, and the serum was discontinued for the day. He died at 4 a. m. on May 17. Necropsy was not permitted.

CASE 28.—M. P., a woman aged 46, was admitted to the hospital on Oct. 27, 1933, with compound fracture of the right leg, acute pharyngitis and a temperature of 104.8 F. Concentrated streptococcus serum (New York state) was given in divided doses on October 28 to a total of 37,000 units and was continued from October 30 to November 5, at which time the infection seemed to be controlled. After a transfusion on November 8, an operative revision of a slough was undertaken on November 10 and another on November 14. Evidence of renewed local inflammation led to the request for further serum therapy, and this was begun on November 15 and continued almost daily to the end. Soluble phenobarbital U. S. P. (sodium phenobarbital) was given on November 1 and November 3; sodium amytal was given, beginning on November 10, for distressing pain

in the leg, and the doses of barbiturates were considerably increased after a further surgical revision of the wound in the leg on December 8. The danger of barbiturate therapy was not appreciated at that time (November 1933).

The blood count on November 6 showed 2,800,000 erythrocytes and 48 per cent hemoglobin; 12,550 leukocytes and 82 per cent of polymorphonuclears. On November 9, after transfusion on the previous day, the erythrocytes numbered 3,150,000 and the hemoglobin was 62 per cent; the leukocytes numbered 7,850, with 72 per cent polymorphonuclears. On November 22, twelve days after the administration of sodium amytal was started, the leukocyte count was 4,100, with 11 per cent polymorphonuclears. Pentnucleotide was given. On November 27 the leukocyte count was 4,800, with 36 per cent polymorphonuclears, and on November 29 it was 7,700, with 38 per cent polymorphonuclears. After the operation on

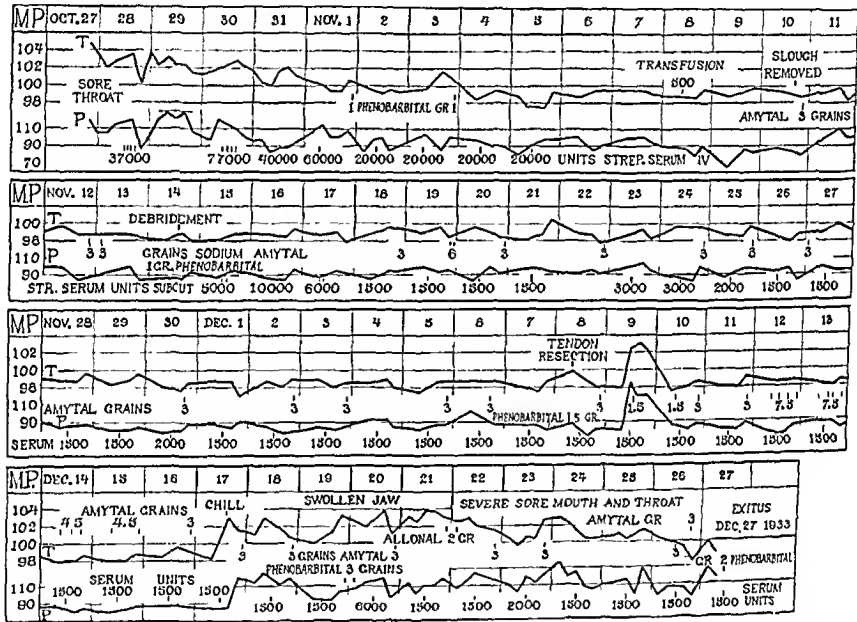


Chart 2 (case 28).—Abridged clinical record of M. P., a woman aged 46. The infection present on admission seemed to respond well to serum therapy, and the recrudescences of the infection following surgical treatment of the leg on November 10, November 14 and December 8 seemed to be controlled in a satisfactory manner. Agranulocytosis became evident on November 22, and this was evidently the chief factor in bringing about the fatal termination.

December 8 the dose of sodium amytal was increased somewhat. Examinations of the blood disclosed a progressive fall of the percentage of polymorphonuclear leukocytes, as follows:

Date	Leukocytes	Polymorpho- nuclears, %
Dec. 11.....	4,050	54
Dec. 13.....	8,850	42
Dec. 14.....	8,250	17
Dec. 15.....	7,500	16
Dec. 16.....	6,400	2
Dec. 18.....	3,250	0

After this date polymorphonuclear leukocytes were not again seen in the blood of this patient. On December 20 the gums became swollen and painful. Progressive ulceration soon appeared in the mouth and pharynx, and the tissues about the lower jaw and the neck became swollen. On December 21 perianal edema was noted. The patient died December 27. At necropsy there was extensive ulceration in the mouth, the pharynx, the small intestine and the large intestine, with hemorrhage into the intestine. The total amount of streptococcus serum used in this case was 624,000 units. It is evident that the serum did not furnish protection from the dangers of toxic agranulocytosis.

CASE 91.—P. F., a man aged 58, was admitted to the hospital on May 17, 1937, with aortic vegetative endocarditis, *Str. viridans* in the blood stream, aphasia and residual hemiplegia from a cerebral insult which had occurred about April 10, 1937. In conjunction with other therapeutic measures, small doses of streptococcus serum (Parke, Davis & Co., biological 2005) were given daily without any evident effect. After a second stroke, on June 23, the patient died on July 7. Necropsy disclosed active vegetations on the aortic valve, bilateral softening of the internal capsule of the cerebrum, due to embolic block of both middle cerebral arteries, old on the left side and more recent on the right side.

CASE 53.—R. N., a man aged 62, was admitted to the hospital on Feb. 8, 1935, because there had been a discharge from his left ear since Dec. 8, 1934. Mastoidectomy was performed on the day of admission, and culture of material from the mastoid gave a growth of hemolytic streptococci. On February 10 the patient had a chill. A culture of the blood made on February 11 gave a positive growth of hemolytic streptococci, about twelve colonies per cubic centimeter of blood. On February 12 the left jugular vein was resected, the mastoidectomy wound was reopened and a transfusion of 500 cc. was given. On February 14 there was clinical evidence of pneumonia and of periarticular inflammation at the left knee. On February 15 another culture of the blood was made, which yielded bacteria. On this day a transfusion of 250 cc. was given and concentrated streptococcus serum (New York state) was administered, 20,000 units subcutaneously and 20,000 units intravenously. On February 16 a culture of the blood was made and yielded 400 colonies per cubic centimeter of blood. Concentrated streptococcus serum (New York state), 20,000 units, was given intravenously. The patient died at 9 a. m., February 17.

CASE 60.—Z. R., a man aged 62, was admitted to the hospital April 23, 1935, with redness and swelling of the skin over the back, extending from the shoulders to the waistline, and a sloughing ulcer over the left scapula at the site of a surgical wound where a papillary nevus had been removed on April 18, 1935. On April 24 exudate from the wound showed streptococci on microscopic examination, and the culture subsequently produced colonies of hemolytic streptococci. The urine contained 5.2 per cent sugar on April 24. A culture of the blood made on the same day remained sterile. A transfusion of 330 cc. and regular (unconcentrated) streptococcus serum (New York state), 25,000 units, were given on April 24, and the same dose of serum was given again on April 25. The patient died at 3:25 p. m., with signs of gradually increasing pulmonary edema. Necropsy was not permitted.

CASE 50.—J. B., a woman aged 80, was admitted to the hospital on Jan. 4, 1935. Mastoidectomy was performed on January 6. After the operation the temperature rose, reaching 106 F. on January 9. On this day a spinal tap yielded cloudy fluid containing 2,500 white cells per cubic millimeter and also microscopically visible streptococci. Serum therapy was requested on January 11, and

regular unconcentrated streptococcus serum (New York state) was given on January 11, 12 and 13 to a total amount of 38,000 units. Death occurred at 2:40 a. m. January 14. Necropsy was not permitted.

These brief notes on the cases in which death occurred are sufficient to indicate the desperate situation at the beginning of serum therapy in many of them. Such treatment represented little more than a gesture or perhaps a forlorn hope for the patients with meningitis (cases 33, 41, 82, 72, 81 and 50) and those with generalized peritonitis (cases 67, 43, 2 and 5). Certainly little or nothing was to be expected in the treatment of the patient in case 49, with terminal streptococcic sepsis after pericardostomy for staphylococcic sepsis; in that of the patient in case 84, suffering from leukemia and gangrenous stomatitis, or in that of the patient in case 91 with vegetative endocarditis and hemiplegia. In cases 62 and 56 the dose of serum was reduced or discontinued after culture of the blood became sterile, and the patients died of pneumonia, probably of septic origin. In case 28 the streptococcic infection was controlled, but the patient succumbed, death being due apparently to toxic agranulocytosis. In case 47, in which the patient had puerperal fever and pneumonia, the specific diagnosis of streptococcic infection was uncertain, and the serum was administered as a forlorn hope on the eve of her death. In 3 instances, although serum therapy was initiated rather late, one has to acknowledge frank failure (cases 90, 53 and 60). There was no attempt to select favorable cases and no thought of refusal to undertake serum therapy because of the desperate or even apparently hopeless nature of the condition.

The 56 patients who survived had various clinical conditions. In subsequent papers we plan to discuss these in special groups according to the region of the body primarily involved. However, it seems best to discuss a few of the successful cases at this place in order to illustrate the technical procedure and to indicate what may be expected from the use of a serum under more fortunate circumstances.

CASE 32.—H. H., a girl aged 2½ years, was admitted to the hospital on Dec. 18, 1933. On December 4 she had an infection of the left index finger, and since December 11 there had been a swollen gland in the left side of the neck and some fever every day. On December 18 the right elbow became swollen. On admission there were old infected lesions on both index fingers and a tender swelling about the right elbow, with limitation of motion. There was a red area on the lateral aspect, which appeared to be the pointing of an abscess. The tonsils were enlarged and inflamed. The temperature on admission was 104.8 F. A culture of the blood made December 18 gave a growth of streptococci with narrow zones of hemolysis. The urine contained a trace of protein and 20 to 30 leukocytes per high power microscopic field. Roentgenologic examination did not reveal any changes in bone. On December 20 a paracentesis of the right elbow failed to obtain any pus. Concentrated streptococcus serum (New York state), 20,000 units, was given subcutaneously, without reaction. A culture of the blood made on this day remained sterile. On December 21 a transfusion of 225 cc. was given. On December 22

another subcutaneous injection of the same serum, 20,000 units, was given. A culture of the blood made on this day remained sterile. By December 26 the swelling of the elbow and of the cervical gland had subsided. On December 30 an erythematous rash appeared on the left arm and the left thigh, and this was generalized on December 31 and January 1. Fever was present on January 1. This was evidently the manifestation of serum disease. The rash promptly subsided, and the temperature remained normal after January 2.

CASE 73.—D. B., a woman aged 22, was admitted to the hospital on Feb. 7, 1936. She had an infection of the upper respiratory tract about January 31 and classic pneumonia on February 4. On admission she was semicomatose. The respiratory rate was 26, the pulse rate 100 and the temperature 100.4 F. The left side of the chest was dull to percussion everywhere posteriorly. The heart sounds were pure; the rhythm was regular, and the blood pressure was 95 systolic and 60 diastolic. The leukocyte count was 24,350, with 95 per cent polymorphonuclears. Examination of the sputum revealed hemolytic streptococci in almost pure culture. On February 9 at 2 p. m. a thoracentesis (on the left) yielded 450 cc. of cloudy yellow fluid, thoracentesis was repeated at 10 p. m., when 650 cc. of fluid was removed. Culture of these fluids yielded hemolytic streptococci. On February 10 a culture of the blood was made, and this also gave a positive growth of hemolytic

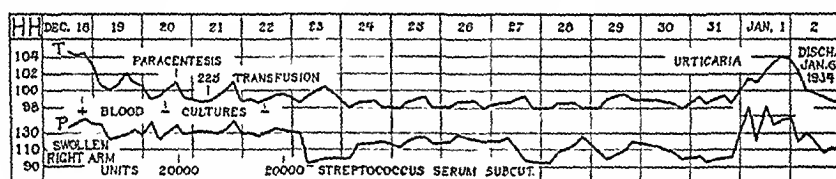


Chart 3 (case 32).—Abridged clinical record of H. H., a girl aged 2½ years. This child was admitted with bacteremia apparently originating from infection of the fingers. The progress of the case was satisfactory, but it is uncertain whether the patient might not have done well without the serum. The fever and rash on December 31 were evidently manifestations of serum disease. They subsided promptly.

streptococci. The white cell count was now 42,800. At this point serum therapy was requested, and the serum³ was administered as follows on February 10:

- 5:21 p. m. 0.1 cc. of 1:10 dilution intracutaneously; reaction negative
- 5:32 p. m. 2.0 cc. of 1:10 dilution subcutaneously
- 5:45 p. m. 3.0 cc. of 1:10 dilution into muscle
- 5:58 p. m. 5.0 cc. of 1:10 dilution into muscle
- 6:12 p. m. 1.5 cc. undiluted into muscle
- 6:27 p. m. 3.5 cc. undiluted into muscle
- 6:38 p. m. 1.0 cc. of 1:10 dilution intravenously
- 6:47 p. m. 3.0 cc. of 1:10 dilution intravenously
- 7:01 p. m. 6.0 cc. of 1:10 dilution intravenously
- 7:16 p. m. 3.0 cc. of 50 per cent dilution intravenously
- 7:29 p. m. 7.0 cc. of 50 per cent dilution intravenously
- 7:46 p. m. 7.0 cc. of undiluted serum intravenously
- 8:00 p. m. 10.0 cc. of undiluted serum intravenously

3. The concentrated streptococcus serum of Parke, Davis & Co. (biological 2005) was used throughout for this patient.

Thus in thirteen doses at approximate intervals of fifteen minutes a total equivalent to about 30 cc. of the undiluted serum was given during two hours and thirty-nine minutes. Fifteen minutes after the last injection the patient had a chill which lasted forty minutes. Oxygen and epinephrine were administered. The temperature rose during the chill to 106.8 F. The patient then began to perspire freely, and the temperature fell to 101 F. in four hours.

This type of reaction we consider favorable. It seems to be identical with the reaction observed frequently when an infection of the blood stream is successfully treated by progressive series of intravenous injections of potent bacteriophage. It also seems to be the same as the reaction observed by Young⁴ and his collaborators when they injected intravenously the amount of mercurochrome suitable to initiate recovery in septic patients. One is therefore inclined to think that this visible

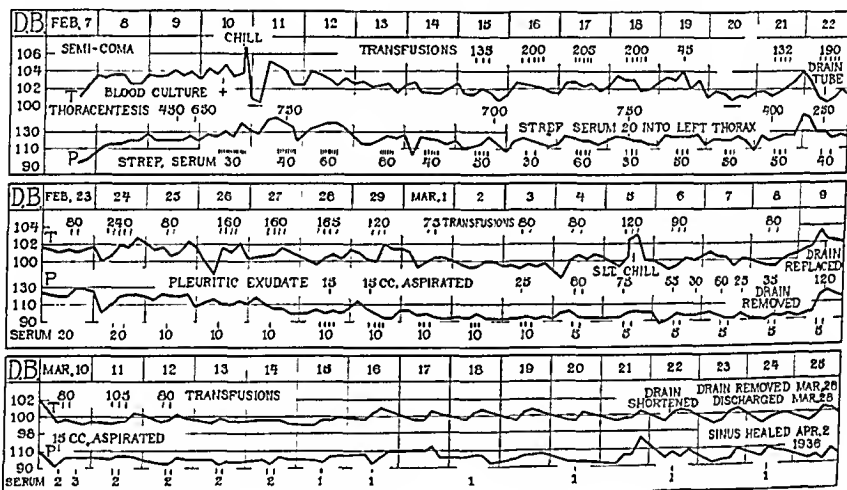


Chart 4 (case 73)—Abridged clinical record of D. B., a woman aged 22. There were pneumonia of the left lung and empyema on admission, and the prognosis was grave on February 10, at which time serum therapy was requested. The series of intravenous injections of serum on this day was followed by a shock reaction (Hugh Young reaction) which marked the turning point in the disease. Desperate measures, however, were still required for its control. After several taps, a drainage tube was inserted into the pleural cavity on February 22. Continuation of the intravenous serum and the fractional transfusions are indicated on the chart. The final result was most gratifying.

reaction is the external manifestation which indicates a turning of the balance in the fight between the bacteria on the one hand and the protective body fluids and phagocytic cells on the other hand, probably due to an injury inflicted on the invading bacteria by the therapeutic agent.

4. Young, H. H.: The Treatment of Infections—General, Local and Urinary—with the Intravenous Injection of Mercurochrome, *Surg., Gynec. & Obst.* 40: 97-104 (Jan.) 1925.

be it serum, phage or chemical poison. As one gets more experience in the intravenous administration of such therapeutic agents one learns to expect this reaction as the culmination of the series of progressively increasing intravenous injections. The prolonged vigorous chill with its distressing cyanosis and air hunger, the high elevation of the temperature and the sudden reddening warmth of the skin at the end, followed by drenching sweat and a spontaneous fall in temperature, constitute a reactive phenomenon so often repeated in successive cases as eventually to be recognized as a distinct reaction to effective intravenous therapy for bacteremia. Undoubtedly this reaction has much in common with the ordinary spontaneous chill, temperature spike and sweat so often repeated in untreated septic disease and in the earlier weeks of malaria, and one may sometimes be unable to distinguish between such reactions when giving intravenous treatment. The timing is, however, significant, and if the therapeutic injections are given in regularly and gradually increasing doses at regular intervals until the chill appears, the true nature of the phenomenon will usually become manifest. Without pretending that this is in any just sense a new phenomenon, we nevertheless believe that the association of this reaction with intravenous therapy directed against the infecting microbe in bacteremia is something which belongs essentially to the more modern era in therapeutics, and we therefore suggest that this rather typical series of manifestations marking the successful termination of a series of intravenous injections be designated as the Hugh Young reaction. A further proof of the character of this phenomenon is of course furnished by the subsequent steady improvement in the clinical condition of the patient and the eventual complete recovery, which is, however, not to be expected without further intelligent and adequate care.

For the patient at present under consideration the ominous return to a temperature of 105 F. at 8 a. m. on February 11 served as a warning against premature relaxation of therapeutic efforts. On this day eight intravenous injections of equal amounts of serum were given at intervals of approximately one hour, to a total amount of 40 cc. For convenience of injection through a needle of gage 27 the serum was diluted with an equal volume of sterile saline solution. Late in the afternoon the chest was again tapped, and 750 cc. of fluid was removed. The patient was more alert and cooperative. As shown in the chart, the large doses of serum were continued every day. The patient did so well that there was some hope of avoiding surgical drainage of the thorax. Beginning on February 15, fractional transfusions were given almost every day until March 12. The left pleural cavity was tapped again on February 18, and 750 cc. of thin, purulent fluid was obtained. It was decided to insert a rubber tube for continuous drainage of the pleural cavity. On February 21, accordingly, a trocar was introduced, and a rubber drain was inserted through the cannula. About 400 cc. of a moderately thick, greenish purulent fluid was obtained at this time, and abundant purulent drainage continued to come away through the rubber tube. Irrigation of the pleural cavity with a proprietary solution of sodium hypochlorite and saline solution was practiced daily beginning on February 27. A roentgenogram taken on

February 27 showed partial collapse of the left lung with consolidation of the lower lobe, moderate pleural exudate at the base and a well established pneumothorax. The drainage tube was shortened from time to time and was removed on March 8. However, because of evident accumulation of fluid and a rise in temperature and in pulse rate the tube was again inserted on the following day, when 120 cc. of purulent fluid was obtained. After progressive shortening of the tube it was finally dispensed with on March 26, and the patient was discharged March 28. She returned to receive an injection of serum on April 2, at which time the thoracic opening was found to be closed and entirely covered by epidermis, so that no further dressing was required.

This patient was able to take large amounts of the serum in divided doses. She became moderately sensitive to the serum, and a moderate rash appeared on February 20, but the diminution in amount of serum after February 22 was made not because of her sensitivity but rather because of economic considerations. The outcome was unexpectedly satisfactory. There is only a small scar, and the patient has remained in excellent condition since leaving the hospital. The total amount of concentrated streptococcus serum used was 760 cc., and the total amount of human blood used in transfusions was 2,902 cc.

CASE 66.—C. R., a man aged 56, was admitted to the hospital on March 28, 1935, with carcinoma of the glans penis. He had worked at shoveling coal for twenty years. On April 17 amputation through the middle of the shaft and bilateral dissection of the inguinal nodes were performed. Examination of the specimens revealed squamous cell carcinoma of the glans and metastatic extension to the right inguinal nodes. There was considerable postoperative edema, but the patient was out of bed by April 29 and was apparently in good condition. On May 3 the temperature suddenly rose to 104 F. The wounds appeared clean, but there was considerable edema of the scrotum and stump of the penis. On May 4 exudate from both inguinal wounds was taken for bacteriologic study. That from the left side was sterile, but that from the right side yielded a growth of hemolytic streptococci. Culture of material taken from the left inguinal wound on May 8 also gave a growth of the same organism. On May 9 the temperature rose again and remained elevated. Brawny, dark red induration extended to the thighs on May 15. Regular (unconcentrated) streptococcus serum (New York state) was given in divided doses on May 16, intracutaneously at 3:10 p. m., subcutaneously at 3:30 p. m., intramuscularly at 3:45 p. m. and intravenously at 3:55 p. m., 4:05 p. m. and 4:30 p. m., to a total amount of 25,000 units. No reaction occurred. The patient was evidently improved by the next day, and the serum was discontinued. On May 20, another ampule of the same unconcentrated serum (5,000 units) was given intravenously without evident reaction. The patient did well until May 26, when again the temperature rose, and there was an extension of the cellulitis to the lower part of the right leg, which became swollen, red and hot on the morning of May 29. The same serum was again administered, this time in divided doses to guard against anaphylactic shock, to a total amount of 15,000 units. Improvement followed at once, but this time the injections of serum were continued daily until June 2. The patient was discharged on June 3 in good condition.

CASE 36.—P. W., a man aged 37, was admitted to the hospital on Jan. 21, 1934, and a bilateral Bassini herniotomy was performed on January 22. The temperature rose to 104.4 F. on January 23. Cultures of material from the operative wounds were made on January 24 and showed abundant hemolytic streptococci, which were found partially susceptible to streptococcus bacteriophage. On January 26 the bacteriophage was applied to the wounds through the drainage tubes

at 3:15 p. m. and again at 6 p. m. and 7 p. m. At 7 p. m. concentrated anti-streptococcus serum (New York state) was given intramuscularly (40,000 units). At 8 p. m. a culture of the blood was made, which remained sterile. After midnight, the bacteriophage was given through the drainage tubes, at 12:45 a. m., 3 a. m., 6 a. m., 9 a. m. and 12 noon on January 27. The concentrated serum, 40,000 units, was given intramuscularly at 1 p. m. No further serum was used, but the local application of the bacteriophage preparation was continued several times each day until February 3, when this also was discontinued. The further course was uneventful, and the patient was discharged February 12 in good condition.

CASE 86.—R. W., a woman aged 54, was admitted to the hospital on Jan. 28, 1937, with signs of extensive cellulitis of the right arm and forearm. A culture of the blood, made at about 3 p. m. on January 28, showed the next day a positive growth of hemolytic streptococci. At 12 noon on January 29 another culture was made, and this one remained sterile. Immediately afterward, streptococcus serum (Parke, Davis & Co., biological 2005) was given, 0.05 cc. into the skin at 12:05 p. m., a subcutaneous injection of 0.5 cc. at 12:07 and another of 1 cc. at 12:32 p. m.; an intramuscular injection of 0.5 cc. serum

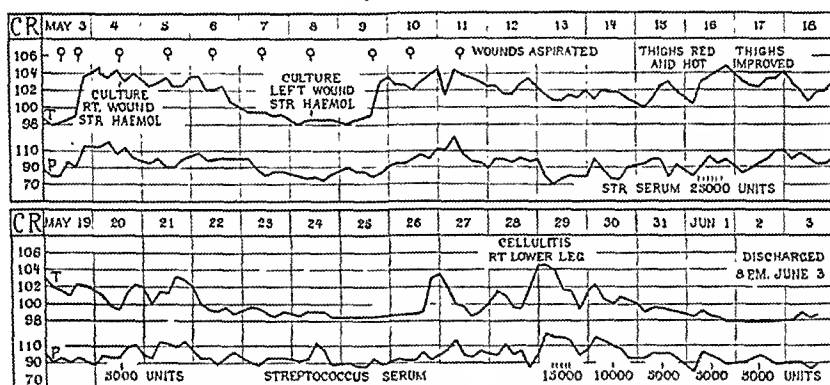


Chart 5 (case 66).—Abridged clinical record of C. R., a man aged 56, with infection of the wound following radical operation for carcinoma of the glans penis and inguinal metastasis. The favorable response to serum given on May 16 and May 20 was followed by a further extension of the inflammation on May 26, which promptly receded when further serum was given.

at 1:22 p. m., another of 1 cc. at 2:10 p. m. and another of 2 cc. at 3:12 p. m.; an intravenous injection of 0.1 cc. at 3:38 p. m., another of 0.2 cc. at 4:13 p. m., another of 0.3 cc. at 4:40 p. m. and another of 0.4 cc. at 4:55 p. m.—making a total of 6.05 cc. of serum for the day. All the doses except the first were diluted with a suitable amount of salt solution to facilitate injection through a fine needle. On the same day administration of sulfanilamide was started, 5 grains at 1 p. m. and 5 grains at 5 p. m. On January 30 the patient received 3 cc. of serum intravenously in four spaced injections and 15 grains of sulfanilamide by mouth. The serum was continued in daily amounts of 1 cc. from January 31 through February 9. The sulfanilamide was discontinued after February 1. Urticaria appeared on this day. The inflammation of the right arm had receded. The patient was discharged in good condition on February 19.

These 5 successful cases have been selected in order to illustrate the use of the serum under varied conditions. Case 32 presented an example

of temporary invasion of the blood stream from lesions on the hands, treated by subcutaneous injections of concentrated state serum to a total amount of 40,000 units. The patient recovered promptly from the infection and had a moderate serum rash ten days after the first injection of serum. The patient in case 73, a young woman desperately ill with streptococcic pneumonia, empyema and bacteremia, was treated with polyvalent streptococcus serum of Parke, Davis & Co., biological 2005, in large doses from February 10 to April 2, the total amount of serum used being 760 cc.; this treatment was augmented by multiple transfusions and surgical drainage of the pleural cavity. The patient in case 66, a man aged 56 with postoperative streptococcic infection, was treated with the regular (unconcentrated) serum of the New York state

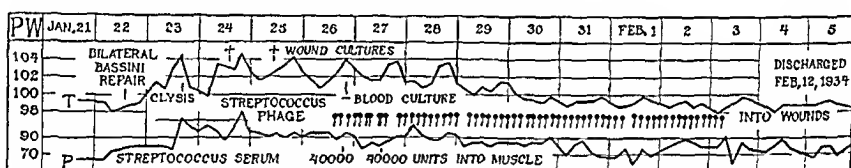


Chart 6 (case 36).—Abridged clinical record of a man aged 37, with streptococcic infection of the wound following repair of hernia. The serum was given by intramuscular injection, and a streptococcus bacteriophage was used for local application to the wound. The result was satisfactory.

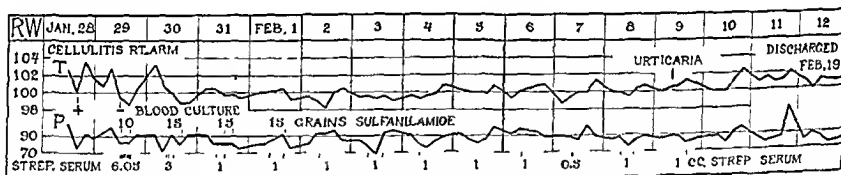


Chart 7 (case 86).—Abridged clinical record of R. W., with cellulitis of the right arm and bacteremia. Relatively small doses of sulfanilamide and of streptococcus serum were used, with very satisfactory results.

department of health. The first administration of the serum, on May 16, to a total of 25,000 units, was quickly followed by improvement of the patient's condition. An injection of 5,000 units of the serum was given on May 20. After a period of improvement there were a relapse and extension of the inflammation, and on May 29 more of the same serum was given in divided doses, to a total amount of 15,000 units. This was followed by 10,000 units on May 30 and 5,000 units on each of three days, May 31, June 1 and June 2. This time there was prompt improvement without further relapse. The patient in case 36 was a man aged 37, with postoperative streptococcic infection. On January 26 a streptococcus bacteriophage was applied to the wounds, and concentrated streptococcus serum (New York state), 40,000 units, was given intramuscularly on each of two days, January 26 and 27. The local bacteri-

ophage treatment was continued, and recovery was rapid. The patient in case 86 was treated with sulfanilamide in moderate doses for four days and with streptococcus serum (Parke, Davis & Co., biological 2005) on these four days and for eight days thereafter. She made a rapid recovery. We have, therefore, 1 patient who was treated with the concentrated streptococcus serum of the New York state department of health; 1 treated with the concentrated streptococcus serum, biological 2005, of Parke, Davis & Co.; a third treated with regular (unconcentrated) streptococcus serum of the New York state department of health; a fourth treated with concentrated streptococcus serum of the New York state department of health and local application of streptococcus bacteriophage; and a fifth treated with the streptococcus serum, biological 2005, of Parke, Davis & Co. supplemented with sulfanilamide. It is evident, therefore, that success may sometimes be achieved with any one of these three serum products, and it is probable that other serums would give similar results if used in the same way, in large doses continued over a sufficient period of time. It is also evident that there is no incompatibility between the serum and sulfanilamide or streptococcus bacteriophage employed simultaneously. There is even reason to hope that superior results may be obtained by the careful use of these agents in combination.

SUMMARY

Preliminary data are presented on 66 additional patients treated with streptococcus serum. We have previously reported the first 26 cases of our entire series of 92.

Severe streptococcus infection respects neither sex nor any age period. The youngest patient in our complete series was 19 days old and the oldest 80 years.

Of the 66 patients in the present group, 18 died. A brief account of each of the fatalities has been recited. There were 6 patients with diffuse bacterial meningitis and 2 with generalized peritonitis, types of disease in which the serum at present available does not offer much hope. In only 3 of the 18 cases was the effect of the serum really disappointing.

Five cases have been selected from the 48 in which the patients recovered, and these have been briefly presented as examples of treatment with three different preparations of streptococcus serum and of serum therapy in combination with multiple transfusions, with bacteriophage and with sulfanilamide, combinations which seem promising.

It is proposed to designate as the Hugh Young reaction the chill, sudden rise in temperature, diaphoresis and fall in temperature so often observed in the treatment of sepsis when an adequate amount of the antibacterial agent, be it a chemical, a bacteriophage or a serum, has been introduced into the blood stream to initiate the eradication of the infecting bacteria.

HEPATIC DAMAGE IN BILIARY DISEASE
ITS RELATION TO THE CONCENTRATION OF BILE ACIDS
IN THE BILE

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It seems plausible that the decrease in the capacity of the liver to concentrate bile acids (taurocholic and glycocholic acids and their salts) in the bile should be an index to the amount of hepatic damage present. Bollman and Mann¹ have shown that bile acids are produced, destroyed and concentrated in and only by the liver. Smyth and Whipple,² as well as Bollman and Mann, have shown that small doses of substances known to be hepatotoxins, that is, chloroform, carbon tetrachloride and tetrachlorethylene, inhibit the function of the liver of the dog in producing and concentrating bile acids. Walters, Greene, and Frederickson³ studied the constituents of the bile of a series of patients who had been operated on for biliary disease. They noticed that a decrease in the concentration of bile acids in the bile followed operations on the biliary system. Mann and two of us (McGowan and Bollman⁴) con-

From the Division of Surgery of the Mayo Clinic (Drs. Gray, McGowan and Nettletrour) and the Division of Experimental Medicine of the Mayo Foundation (Dr. Bollman).

1. Bollman, J. L., and Mann, F. C.: *The Influence of the Liver in the Formation and Destruction of Bile Salts*, *Am. J. Physiol.* **116**:214-224 (June) 1936.

2. Smyth, F. S., and Whipple, G. H.: *Bile Salt Metabolism: I. Influence of Chloroform and Phosphorus on Bile Fistula Dogs; II Proteose and X-Ray Intoxication: Thyroid and Thyroxin*, *J. Biol. Chem.* **59**:623-646 (April) 1924.

3. Walters, W.; Greene, C. H., and Frederickson, C. H.: *The Composition of the Bile Following the Relief of Biliary Obstruction: Report of a Series of Illustrative Cases*, *Ann. Surg.* **91**:686-693 (May) 1930.

4. McGowan, J. M.; Bollman, J. L., and Mann, F. C.: *The Bile Acids in Icterus Produced by Toluylenediamine*, *J. Pharmacol. & Exper. Therap.* **58**:305-311 (Nov.) 1936.

firmed these findings with dogs. Ravdin, Johnston, Riegel and Wright⁵ have shown that bile salts are always absent from the hepatic bile after the common bile duct has been completely obstructed for a week or more and that the reappearance of such bile salts in the hepatic bile takes place only after a variable but considerable period.

Many patients with biliary disease have varying amounts of obstruction at the lower end of the common bile duct as a result of pancreatitis or spasm of the sphincter of Oddi, as has been demonstrated roentgenologically by Walters and Thiessen⁶ and by means of studies of intrabiliary pressure by Butsch, Walters and one of us (McGowan).⁷

One would expect that improvement in hepatic function would occur as a result of the decompressing effect of T tube drainage. We attempted to correlate the reduction in concentration of bile acids with hepatic damage as evidenced by clinical or pathologic examination and to demonstrate improvement, if any, in hepatic function as a result of T tube drainage by frequent determinations of the concentration of bile acids in the bile.

METHODS OF STUDY

We studied 50 cases in which the common bile duct had been explored at the time of operation and in which prolonged biliary drainage by means of a T tube had been found necessary. The bile was collected in daily twenty-four hour specimens; it was thoroughly mixed, and a sample was placed in the refrigerator until the analysis was made. Bile acid concentration was determined according to the method of Gregory and Pascoe.⁸ It was then attempted to correlate the bile acid concentration with the amount of clinical and pathologic evidence of hepatic damage.

The degree of hepatic damage was estimated from the history, from the report of tests for liver function and from the gross and microscopic appearance of the liver at the time of operation.

The chief factor in the history considered indicative of hepatic damage was jaundice. This is in accordance with the observations of

5. Ravdin, I. S.; Johnston, C. G.; Riegel, C., and Wright, S. L.: A Study of Human Liver Bile After Release of Common Duct Obstruction, *J. Clin. Investigation* **12**:659-672 (July) 1933.

6. Walters, W., and Thiessen, N. W.: Visual Methods of Studying the Physiology of the Common Bile Duct: I. The Problem of Pancreatitis and Sphincteritis, *Proc. Staff Meet., Mayo Clin.* **9**:772-775 (Dec. 19) 1934.

7. McGowan, J. M.; Butsch, W. L., and Walters, W.: Pressure in the Common Bile Duct of Man: Its Relation to Pain Following Cholecystectomy, *J. A. M. A.* **106**:2227-2230 (June 27) 1936.

8. Gregory, R., and Pascoe, T. A.: The Quantitative Determination of Bile Acids by Means of a New Color Reaction and Monochromatic Light, *J. Biol. Chem.* **83**:35-42 (July) 1929.

Snell,⁹ made in a group of cases similar to ours, in which he showed that jaundice severe enough to produce a bilirubin content of 8.3 mg. per hundred cubic centimeters of serum was accompanied by evidence of impaired hepatic function.

The tests of function were the bromsulphalein, Takata-Ara, hippuric acid and galactose tolerance tests.

The degree of damage to the liver was classified as mild, moderate or severe. While we refer to some livers as "normal" or as having suffered no damage, all the patients studied had had biliary disease severe enough to require drainage of the common duct; probably none had escaped at least a minor degree of hepatic damage. In most instances the careful taking of the history gave an accurate index of the condition of the liver. In only 1 case in which the history indicated that hepatic damage was lacking did the test for retention of dye, the result which was graded 4, reveal what proved to be the true

TABLE 1.—*Relation of Hepatic Damage to Concentration of Bile Acids in Bile*

Damage to Liver as Classified by History	Cases	Jaundice (Twice or More), Percentage of Cases	Tests of Hepatic Function Indicating Hepatic Damage, Percentage of Cases	Hepatic Disease Noted by Surgeon, Percentage of Cases	Average Concentration of Bile Acids on Fifteenth Day, Mg. per 100 Cc.
None ("normal").....	21	5	0	20	1,840
Mild.....	11	45	27	43	1,165
Moderate.....	14	65	80	61	512
Severe.....	4	100	100	75	120

state of the liver. A history of jaundice on two occasions was followed by impairment of hepatic function. Patients classified as having severely damaged livers had jaundice at the time of admission, which had been present for periods varying from three weeks to one and a half years.

The duration of other complaints did not parallel the severity of the hepatic damage. Patients with normal livers had symptoms referable to the biliary system for an average of three years, whereas those with mildly, moderately and severely damaged livers had symptoms for an average of six, four and one-half and four years, respectively.

The gross appearance of the liver, while useful in classifying livers as normal, chronically inflamed or definitely cirrhotic, did not give accurate information with regard to the degree of physiologic change which was associated with these pathologic findings.

The percentage of each group of patients showing impairment of hepatic function increased progressively from the patients with mildly damaged livers to those with severely damaged livers.

9. Snell, A. M.: The Effects of Calculous Biliary Obstruction on the Structure and Functions of the Liver, Surg., Gynec. & Obst. **63**:596-602 (Nov.) 1936.

In 20 per cent of cases in which the liver was classified as normal and in 75 per cent of cases in which the damage was classified as severe there was gross pathologic evidence of hepatic disease at operation. This method of classifying hepatic damage, however, is more accurate than the figures indicate. For example, in the normal group the gross changes noted never indicated more severe damage than hepatitis of grade 1, whereas in the more severely damaged group hepatitis of grade 4, or cirrhosis, was frequently evident. When the evidence for hepatic damage was great, the function of that particular liver for concentrating bile acids was found to be low (figs. 1, 2 and 3).

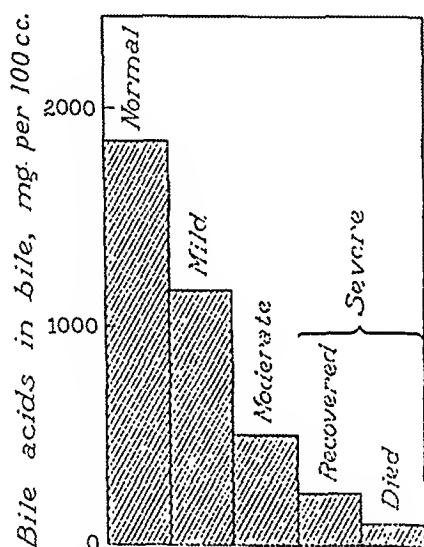


Fig. 1.—Average concentrations of bile acids in the bile of patients with normal livers and of those with clinical evidence of mild, moderate and severe hepatic damage, respectively.

After operation there was a progressive decrease in the concentration of bile acids in the bile of each individual patient. This reached a variable low level on the fourth day after the operation and then gradually rose to a fixed level on the fifteenth to the twenty-first day (fig. 4). Four patients showed improvement even after four weeks of biliary drainage.

Damaged livers did not completely regain their function of concentrating bile acids. This seems to indicate that there is a limit to the extent of recovery after injury. This limit is usually reached at the end of the second week, although improvement has continued much later. In 1 case in which the common bile duct had been com-

pletely obstructed by stricture there was a bile acid concentration of 33.8 mg. per hundred cubic centimeters in the first specimen, collected two hours after the operation. This value rose slowly and was continuing to rise even after one month, when it had reached 500 mg. per hundred cubic centimeters.

REPORT OF CASES

CASE 1.—*Normal liver.*

A man aged 56 complained of repeated attacks of biliary colic of one year's duration. He had never been jaundiced. Cholecystograms demonstrated a normally functioning gallbladder which contained stones. At operation the common duct



Fig. 2.—Section of liver graded clinically as moderately damaged. Biliary obstruction from carcinoma at the head of the pancreas was relieved by T tube drainage. The concentration of bile acids on the fifteenth day after the operation was 360 mg. per hundred cubic centimeters.

was seen to be enlarged to twice its normal size. It contained no stones. The gross appearance of the liver revealed hepatitis of grade 1. The only probable reason for hepatic damage in this case was back pressure on the liver, as indicated by the enlarged common duct and the biliary colic of one year's duration. The mildness of the symptoms, their short duration, the normally functioning gallbladder and the absence of jaundice and also of stones in the common duct would lead one to grade this liver as "near normal." The concentration of bile acids on the third day after the operation was 1,060 mg., and on the twelfth postoperative day 1,430 mg., per hundred cubic centimeters.

CASE 2.—*Severely damaged liver.*

A man aged 75 years had had jaundice with itching for one and a half years. The Takata-Ara test of liver function gave positive results. The hippuric acid test revealed excretion of only 0.64 Gm. of hippuric acid in the urine. The

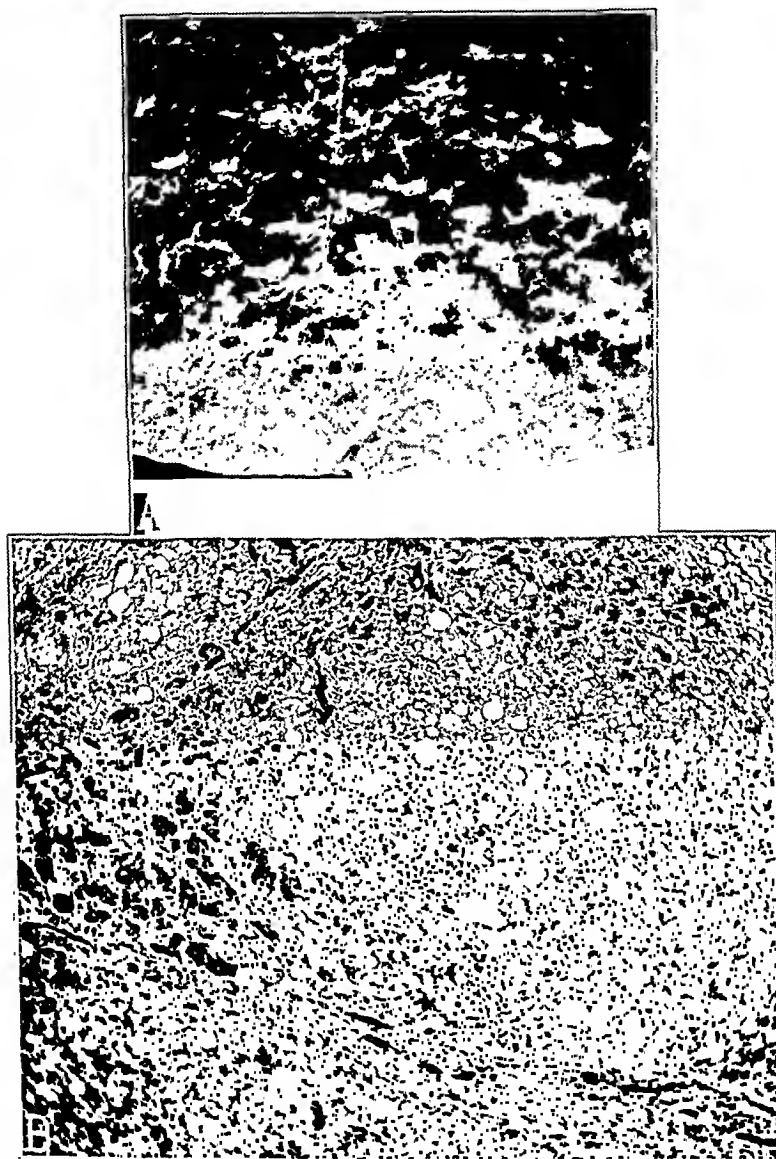


Fig. 3.—A severely damaged liver: *A*, in the gross, and *B*, in microscopic, appearance. Around the lobule is a broad band of fibrosis, mixed with which are scattered islands of parenchymal hepatic cells attempting to regenerate. The hepatic lobule itself consists of a framework with large empty spaces and little evidence of any parenchymal hepatic cells.

bilirubin content of the serum on admission was 8.3 mg. per hundred cubic centimeters; the protein content was 6.3 mg. per hundred cubic centimeters and the albumin-globulin ratio was 1:1.2. At operation a stone was found impacted in the ampulla of Vater. The liver revealed hobnail cirrhosis. The patient made a good recovery, and two weeks after operation choledochograms revealed a patent common duct. The concentration of bile acids on the fifteenth day after the operation was 224 mg. per hundred cubic centimeters.

COMMENT

Two patients with a concentration of bile acids in the bile constantly less than 100 mg. per hundred cubic centimeters died six and eight weeks, respectively, after operation (figs. 1 and 3). Two others, with

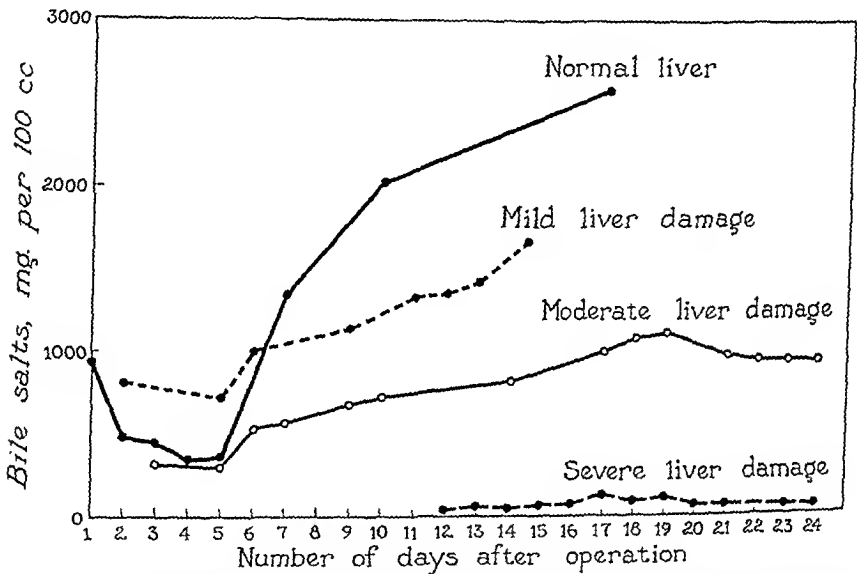


Fig. 4.—Concentrations of bile acids after operation in the bile of a patient with a normal liver and of patients with mildly, moderately and severely damaged livers.

a concentration of bile acids that remained slightly more than 200 mg. per hundred cubic centimeters for more than two weeks, slowly but completely recovered. These cases illustrate the prognostic value of the test. It would seem that when the amount of bile acids is constantly less than 200 mg. per hundred cubic centimeters the liver is severely damaged and the prognosis is grave.

The photomicrograph of the liver of the patient for whom the concentration of bile acids remained less than 100 mg. per hundred cubic centimeters showed destruction of hepatic cells in the center of the lobule and only a few parenchymal hepatic cells toward the periphery of the lobule (fig. 3). In contrast to this, figure 5 represents the

moderately damaged liver of a patient for whom the concentration of bile acids on the tenth day after the first operation, a year previously, was 690 mg. per hundred cubic centimeters and was 685 mg. per hundred cubic centimeters on the fifteenth day after an operation recently performed for stricture, at which time the specimen for biopsy was taken.

The clinical grading of hepatic damage can only be arbitrary, as it is impossible to say when a normal liver changes into a mildly damaged one. However, the evidence derived from a history of jaundice, from recognized tests of liver function and from the gross appearance of

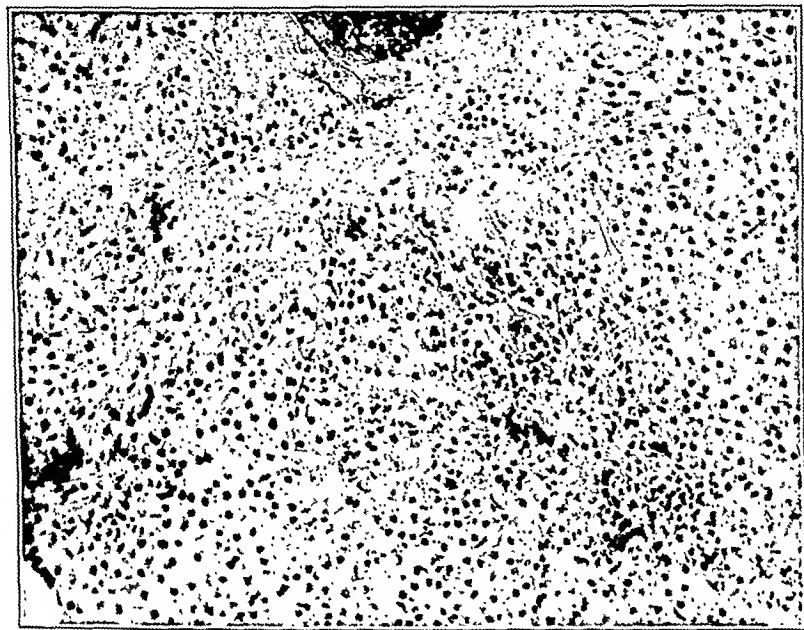


Fig. 5.—Biopsy specimen of a moderately damaged liver. The lower part represents fibrosis of the peripheral lobule and disappearance of parenchymal hepatic cells. Above is parenchymal hepatic tissue with groups of leukocytes indicating infection. The concentration of bile acids on the eleventh day after the operation was 685 mg. per hundred cubic centimeters.

the liver, while negligible for the normal liver, is 100 per cent indicative for the moderately damaged liver.

Paralleling this, the average concentration of bile acids in the bile on the fifteenth day after the operation for the normal liver is 1,840 mg. per hundred cubic centimeters and for the moderately damaged liver is 512 mg. We had only 1 case which proved an exception to this. Clinically the liver of the patient in this case was graded as normal, and grossly it suggested to the surgeon hepatitis of grade 1.

On the fifteenth day after the operation the concentration of bile acids was only 535 mg. per hundred cubic centimeters. However, it later rose to 1,820 mg.

This case illustrates what Smyth and Whipple have brought out in experimental studies on animals. They found that a definite decrease in concentration of the bile acids in bile may be present when neither gross nor microscopic evidence of hepatic damage is shown. The recovery of the ability of the liver to concentrate bile acids, which takes place after the postoperative depression, leads one to believe that such impairment in hepatic function may be only temporary. In cases in which there is gross clinical and pathologic evidence of hepatic damage complete recovery of the ability of the liver to concentrate bile acids does not occur.

The reason for the decrease in concentration of bile acids in the bile after operations on the common duct will need further investigation. The degree of this postoperative decrease in bile acid concentration is extremely variable and does not seem to have any relation to the degree of clinically demonstrable damage to the liver.

An interesting observation in these studies was that patients who had evidence of severe hepatic damage and bile acid concentrations greater than 200 mg. per hundred cubic centimeters on the seventh day after the operation made a slow recovery but apparently recovered almost as well as did those whose livers were apparently more nearly normal. This indicates that they had sufficient functioning hepatic cells to sustain healthy existence under these conditions. This amount of liver is probably represented by a concentration of bile acids greater than 200 mg. per hundred cubic centimeters. Concentrations greater than this and up to 3,000 mg. per hundred cubic centimeters may be spoken of as "liver reserve" (fig. 1).

The 2 patients who had concentrations of bile acids consistently less than 100 mg. per hundred cubic centimeters were up and about two weeks after operation and apart from lassitude, anorexia and persistently high bilirubin values showed no signs of grave hepatic damage (fig. 3).

The improvement in the function of the liver in concentrating bile acids during drainage of the common duct is striking and would seem to be a result of the decompressing effect of relieving tension in the biliary tree (fig. 4). It would seem wise, therefore, to prolong drainage of the common duct until the improvement in concentration of bile acids has ceased and until choledochograms and studies of intrabiliary pressure show the common duct to be unobstructed.

SUMMARY AND CONCLUSIONS

A clinical study was made of 50 cases in which drainage of the common bile duct was established by means of a T tube. The condition of the liver was estimated from the history, from the results of recognized tests of hepatic function and from the gross appearance of the liver at operation. The degree of hepatic damage thus determined was correlated with frequent determinations of the concentration of bile acids in the bile. Low concentrations of bile acids occurred in every case in which there was other evidence of hepatic damage. An inhibition in the function of the liver in concentrating bile acids occurred postoperatively. This inhibition was rapidly recovered from in cases in which the liver was clinically normal, but recovery was slower in those in which the liver had been damaged. A moderately damaged liver may continue to improve slowly even after a month of T tube drainage.

TECHNIC OF THE IVORY IMPLANT FOR CORRECTION OF SADDLE NOSE

MICHAEL M. WOLFE, M.D.

PHILADELPHIA

Much of the beauty of the face depends on the size and symmetry of the nose.¹ The saddle nose attracts the attention of even the most casual observer and is therefore "first of importance to be corrected."²

More than a hundred years ago Castle³ wrote: "The bones of the nose, from their situation are much exposed to fractures. The fragments are sometimes not deranged; but, most frequently they are depressed." The same thought has been expressed by me in a recent article.⁴ Trauma is the most common cause of saddle nose.

Contrary to the opinions of some,⁵ I believe with others⁶ that animal (elephant) ivory offers the ideal implant for the correction of such deformities. Cork⁷ has been employed, although reports of the results after a period of years are not to be found in the literature. Since the chemical composition of cork is purely vegetable the probability of retention of the implant is always uncertain.

Autoplastic materials (bone and cartilage) often produce an abnormal midline ridge, due sometimes to narrowness of the graft but most frequently to absorption. A nose with such a deformity has been referred to as a "keel nose."

1. Warren, J. C., and Gould, A. P.: *International Text-Book of Surgery*, Philadelphia, W. B. Saunders Company, 1900, vol. 2, p. 77.

2. Hays, H.: *Diseases of the Ear, Nose and Throat*, Philadelphia, F. A. Davis Company, 1925, p. 522.

3. Castle, T.: *A Manual of Surgery*, ed. 4, London, E. Cox, 1831, p. 379.

4. Wolfe, M. M.: *Etiology of the Saddle Nose*, *Ann. Otol., Rhin. & Laryng.* **44**:504-509 (June) 1937.

5. Sheehan, J. E.: *Plastic Surgery of the Nose*, New York, Paul B. Hoeber, 1925, p. 8. Carter, W. W.: *Correction of Nasal Deformities by Plastic Methods and by Transplantation of Bone and Cartilage*, *Internat. J. Orthodontia* **19**:1012-1016 (Oct.) 1933.

6. Maliniak, J.: *The Use of Ivory in Rhinoplasty*, *Arch. Otolaryng.* **1**:599-611 (June) 1925. Salinger, S.: *Ivory Implants for Saddle Nose: Results in Fifty Cases*, *Ann. Otol., Rhin. & Laryng.* **40**:801-808 (Sept.) 1931.

7. Priselkov, P. V.: *The Use of Cork in the Surgical Treatment of Saddle Nose*, *Vrach. gaz.* **34**:534-536, 1930. Dahmann, H.: *Cork as a Plastic Material for the Raising of "Saddle Noses," Ztschr. f. Laryng., Rhin., Otol.* **20**:451-457 (March) 1931.

The two stage operation for the correction of saddle nose has been previously described.⁸ In this contribution the one stage operation will be discussed in detail.

Ivory has been employed for almost twenty-five years. It has stood the test of time; it retains its original shape and size, and it possesses the other attributes essential for this type of operation.

For successful results in the correction of a saddle nose, attention to minute details is of paramount importance.

First, one must be absolutely certain that one has genuine elephant ivory. Ivory from young elephants appears to be better conditioned physiologically than does that from old elephants. When treated with concentrated sulfuric acid for fifteen minutes genuine ivory is not affected, while vegetable ivory and walrus tusk⁹ are stained rose color; the tint disappears if the substance is washed in water. The latter two substances are not to be used on account of their irritating qualities and on account of the fact that they are not retained by the host.

A cast of the face is made in all cases of saddle nose. An impression (regular dental impression plaster) is made of the patient's face from the midforehead to and including the upper lip. This permits the patient to breathe through the mouth. To facilitate the removal of the impression, the face is greased with olive oil, heavy petrolatum is applied to cover the eyebrows and eyelashes, and tiny pieces of cotton soaked in olive oil are inserted in both nostrils. When the impression begins to harden it is removed by being raised at the forehead section, with a forward and downward motion. The inner surface of the impression is painted with a thin layer of (dental) shellac, which dries in about fifteen minutes. It is then treated with a thin coat of sandarac, which requires about thirty minutes for drying. The impression is next soaked in cold water for about three to five minutes (until bubbling ceases). This soaking replaces the moisture lost during the hardening (crystallization) of the plaster. The impression is not to be dried after soaking. Modeling plaster is then poured into the impression, and the cast is inverted. As soon as the cast begins to harden, the edges are trimmed with an ordinary pocket knife to discover the line of demarcation, and by a wedging motion the two are separated (fig. 1*A*). Personally, I prefer "artificial stone" for the production of the model; it withstands repeated fittings of the ivory much better than does plaster of paris.

A suitable piece of ivory having been selected, the dorsum of the nose of the cast is smeared with lipstick. The ivory is placed on the

8. Wolfe, M. M.: Plastic Surgery of the Saddle Nose, *Laryngoscope* **43**: 897-904 (Nov.) 1933.

9. Watkins, A. B. K.: Notes on Plastic Surgery, *J. Laryng. & Otol.* **48**:809-820 (Dec.) 1933.

nose, and wherever the lipstick leaves its imprint the ivory is carved. For the carving I employ a rotary motor with carborundum wheels, one flat and the other round. After repeated fitting and carving, the under surface when completed will fit the depression (saddle deformity) with the accuracy of a dental inlay. The superior surface, or what is subsequently to become the new dorsum of the nose, is then carved to a height and width equal to the depth and width of the deformity. It is then drilled with tiny holes. This lightens the implant and permits fibrous bands to grow into the ivory, holding it more securely in position. In every case two pieces of ivory are carved; one to fit the depression

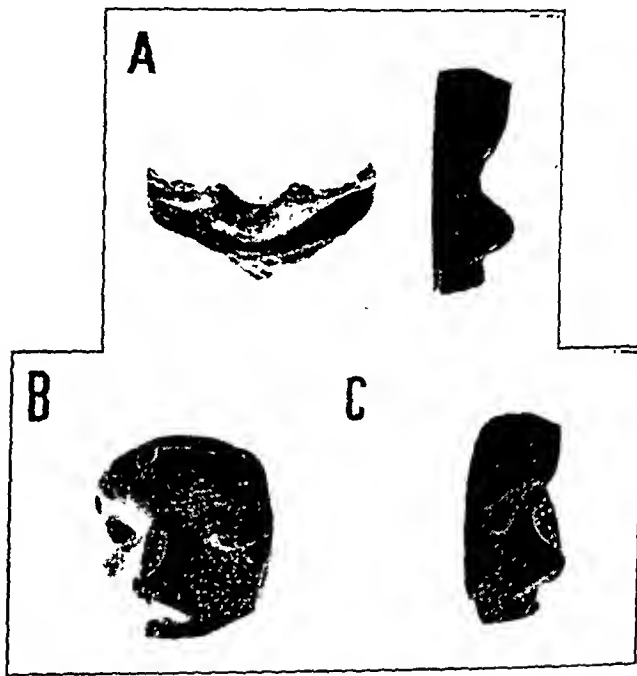


Fig. 1.—*A*, photograph showing the cast after its removal from the impression taken of the patient's face. *B*, ivory implant accurately carved to fit the saddle deformity. *C*, oversized implant most commonly employed for the severe types of saddle nose.

accurately (fig. 1 *B*) and the other slightly oversized (fig. 1 *C*). This is to allow for the thickness of the skin and to insure a better cosmetic result by the trying of two implants. The implants are scrubbed with soap and water to cleanse them and to remove the lipstick. The sharp edges are then made perfectly smooth with a fine sandpaper disk, a dental engine being employed. This is just as important as the actual fit of the implant. A sharp edge is likely to irritate locally, produce a serous exudate and eventuate in expulsion of the implant. Then, too, as in the case of a mild injury, a sharp edge will traumatize the

fibrous enveloping capsule; this will also result in loss of the ivory. All such complications may be entirely eliminated if the implant is properly carved, accurately fitted and smooth on all surfaces.

The implants are wrapped in gauze and sterilized by boiling. The water must be cold; the temperature should be increased slowly. If the temperature of the water is raised too rapidly or if the implant is placed in boiling water, the sudden external expansion of the ivory will cause it to crack, and it then becomes useless. The nurse is instructed to boil the implant for twelve minutes in distilled water. Prolonged boiling has a tendency to remove some of the constituent salts, thereby changing the chemical composition of the ivory and decreasing its resistance to eventual expulsion. Moreover, it is essential to retain all the chemical components of ivory in nearly the original state if the biologic characteristics of the substance are to be preserved.

Many types of outside incision are employed for the insertion of implants. Among them are the superciliary, glabellar, nasion, canthal and columellar incisions, which result in an "almost invisible scar." My own preference has always been to employ the intranasal incision so that no scars are visible.

The preliminary preparation consists of closely clipping the hair in the nostrils with special blunt-pointed scissors with a convex back; this prevents nicking the skin. Crusts and intranasal débris are removed with hydrogen peroxide. The patient washes the face with soap and water to remove grease and cosmetics. The nose is then packed with a 1:8,000 dilution of mercurophen a half-hour before operation. Such a simple preoperative routine has proved to be not only exceedingly effectual but less complicated and less traumatizing than douches for the nose and the use of various antiseptics and germicides.

One hour before operation the patient is given a mild sedative. Morphine alone or in combination with atropine is never employed, on account of the short duration of the operation and the possibility of an idiosyncrasy.

The patient's face is finally prepared on the operating table; this preparation consists of cleansing with alcohol and then with tincture of metaphen in a dilution of 1:200 (untinted), which is removed with alcohol. The nasal packing is removed, the face is draped and the nose is anesthetized. General anesthesia should not be employed in rhinoplastic operations. The postoperative nausea and vomiting incident thereto obviously invite infection. Infiltration hydrochloride anesthesia is the method of choice; a 1 per cent solution of procaine hydrochloride with epinephrine is administered intranasally to the sides and dorsum of the nose.

For insertion of the implant an incision is made within the left vestibule at the inferior border of the triangular cartilage (fig. 2). The length of the incision depends on the size of the implant to be inserted. By blunt dissection with the Joseph comma knife, sufficient skin is separated overlying the dorsal and lateral walls of the nose to produce a pocket for the reception of the ivory. As a general rule there is little bleeding from this dermal separation. After several trials have been made, the implant which best fits the deformity is permitted to remain. The implant must never be touched; it is handled entirely with instruments. The skin overlying the implant must not be on a stretch, as any tension may alter the nutritional supply of the dorsal skin and may defeat the operation. The implant having been adjusted, three strips of adhesive tape are placed over the nose; this constitutes the

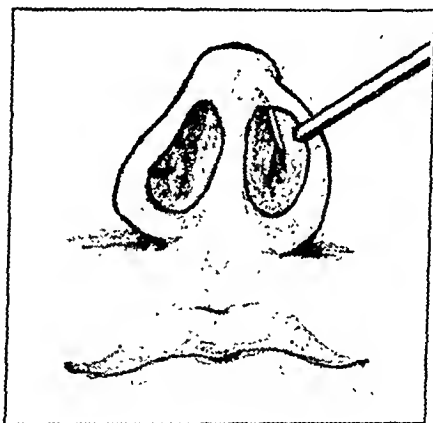


Fig. 2.—Sketch illustrating the incision made within the left vestibule at the inferior border of the triangular cartilage. If the surgeon is left handed, the incision is made on the opposite side. One incision is sufficient.

external dressing. A small piece of gauze treated with petrolatum is placed in the nostril against the line of incision, to keep the wound moist and permit free drainage. Suturing of the line of incision as done by some surgeons not only prevents free drainage but is likely to produce a hematoma, thus inviting infection. The patient is kept quiet in bed for three days in the semireclining position. The petrolatum gauze pack only is changed daily. After the third day the three external strips of adhesive tape are removed, and no further dressings or applications are necessary. By this time the implant is held in position by the overlying skin, which has contracted, and by the accurate fit of the ivory to the dorsum of the nose. The patient rarely complains of any postoperative pain, and the swelling completely subsides in about five days. If the implant has been retained beyond the first week and there are no visible

differences in the appearance of the new nose, the ivory will usually remain in situ indefinitely.

Slight injuries to the nose are usually well tolerated. Even though the trauma is sufficient to produce a local reaction the ivory will remain in place if the fibrous capsule is not disturbed. A severe blow, however, rupturing the fibrous envelop will produce a marked reaction with all the signs and symptoms of acute inflammation and with subsequent expulsion of the implant either at the side of the nasion or through the nasal mucosa. At the first sign of any irritation the implant should be removed via the original incision, and the nose should be drained with a rubber dam for twenty-four to forty-eight hours. When regeneration is completed a new implant may be inserted after a lapse of from six to eight weeks. It is almost superfluous to add that plastic corrections should never be attempted in the presence of any active pathologic



Fig. 3.—Photographs showing result of the implantation. The picture at the left was taken before the operation; that on the right, after the operation.

process in the nose and never before the patient reaches the age of 17, at which time the nose has attained its full growth.

SUMMARY

External incisions of the nose, regardless of their location, always result in scarring, while incisions about the tip have a tendency to destroy its natural contour. The accepted intranasal incision not only is easier of approach but never results in any scarring. It is time that all external incisions for practically all types of nasal corrections were relegated to the scrap heap of plastic operations.

Properly selected ivory taken from a young elephant and carefully carved is of preeminent importance for a good cosmetic result. The overlying skin should never be subjected to any tension. In doubtful cases, in which the dorsal skin is rather firmly attached (as the result of

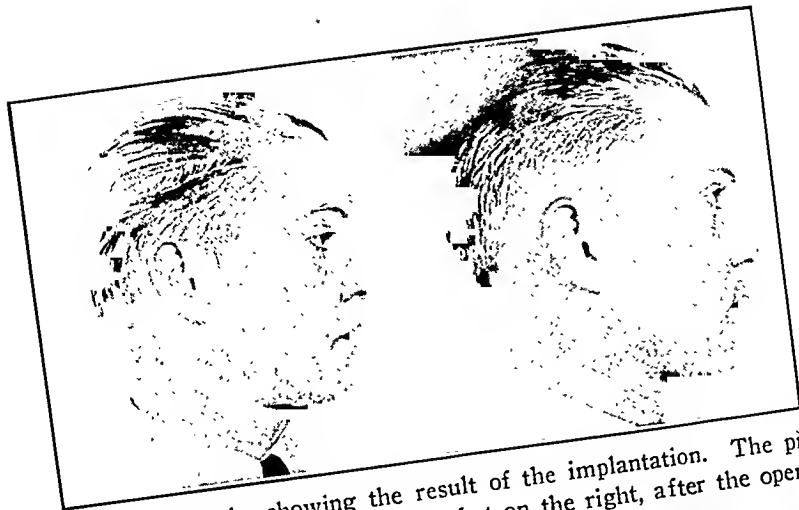


Fig. 4.—Photographs showing the result of the implantation. The picture on the left was taken before the operation; that on the right, after the operation.

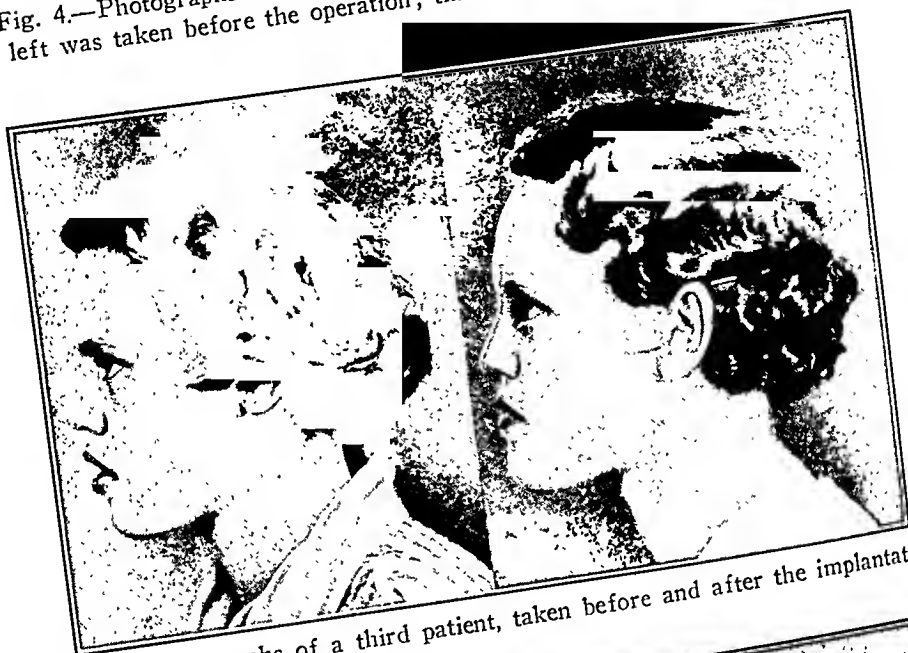


Fig. 5.—Photographs of a third patient, taken before and after the implantation.

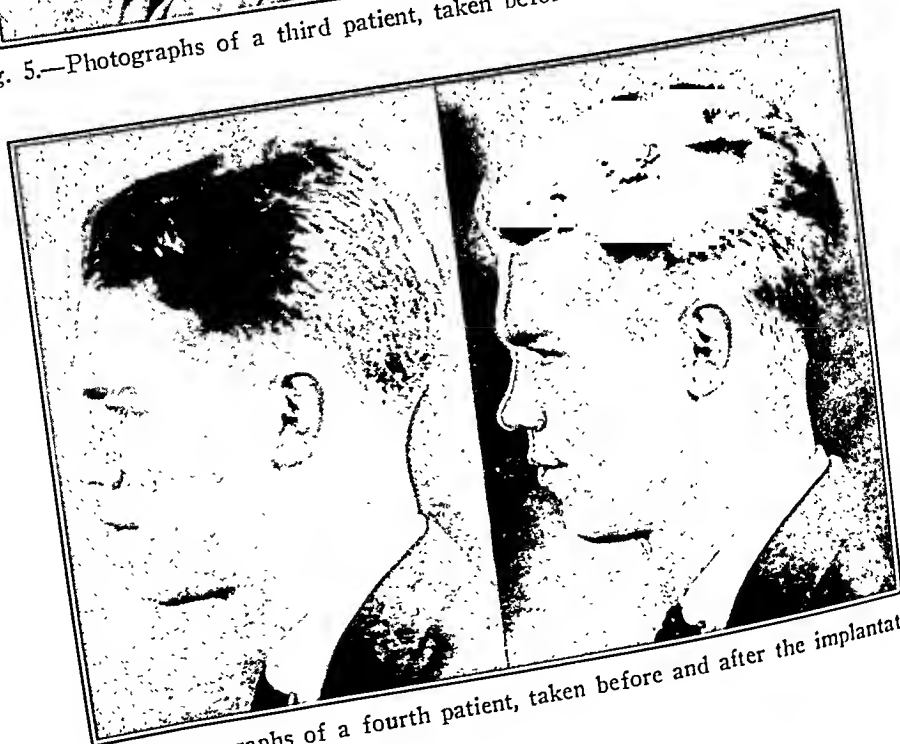


Fig. 6.—Photographs of a fourth patient, taken before and after the implantation.

severe injury or infection), it is better to employ a rather small implant, achieving at least some improvement, than to take the risk of complete failure caused by stretching the skin.

The insertion of the implant is a simple procedure and is quickly accomplished, which is gratifying to the patient. The insertion of an autogenous graft is always attended with some danger; in addition such an operation requires general anesthesia.

The encapsulation of the implant with fibrous tissue seems to be uniform and never distorts the end result. It is known that autogenous implants do become absorbed irregularly and result in various distortions. If the patient is apparently in good health, the nasal orifices free from infection, asepsis and antisepsis rigidly observed, properly carved elephant ivory employed and careful technic used one should have no hesitancy in using this method for the correction of saddle nose.

Any implant which is easily procured, readily prepared, quickly inserted, resistant to infection and well tolerated by the tissues possesses merit of distinction. Elephant ivory is an organic substance the chemical composition of which is similar to that of human bone. This accounts for its nonirritating effect and for the fact that it is not acted on as a foreign body. Moreover, elephant ivory never changes its shape or becomes absorbed. For these reasons, elephant ivory has definitely established its reputation as the ideal implant for the correction of saddle nose.

The Widener Building.

DUODENAL RUPTURES

ALEXANDER LURJE,

IVANOV, U. S. S. R.

Retroperitoneal duodenal tears occupy a particular place among subcutaneous intestinal ruptures of traumatic origin. The integrity of the peritoneum creates diagnostic difficulties during the first hours after the trauma.

According to the statistical reports of Kenn,¹ only 9 of 138 patients with retroperitoneal and intraperitoneal duodenal ruptures recovered. Retroperitoneal ruptures are often overlooked during laparotomy (Gibe²). The presence of retroperitoneal hematoma, emphysema or a green spot on the parietal peritoneum makes the surgeon suspect ruptures of the retroperitoneal hollow organs. The diagnosis is most difficult in cases in which there are injuries of other viscera. In case of blunt trauma to the abdomen, after manipulation of the intestine and other internal organs has been completed the duodenum should be investigated if there are evidences of retroperitoneal hematoma, emphysema or a green spot on the parietal peritoneum. The location of the lower horizontal part of the duodenum on the fixed spinal column in cases of acute trauma predisposes to ruptures of that portion of the duodenum. One may suppose that at the moment of trauma the duodenum represents a bag filled with gas and hermetically closed. On one side the exit from the duodenum is closed by the contracted pylorus, on the other it is closed by the superior mesenteric artery and the root of the mesentery pressing on the flexura duodenojejunalis at the moment of the trauma. The volume of gas, diminishing in the moment of impact, increases the compression, and the intestine bursts. Some particular features of the clinical picture of duodenal tears draw attention in my case, which seem worthy of reporting.

REPORT OF A CASE

Mr. K., a man aged 30, was admitted to the hospital because of a trauma of the abdomen. He had been pressed against a wall by a truck. There was acute abdominal pain. The pulse rate was 48. Cold sweat and shock were present. Palpation established a more or less intense strain of the muscles in

From the Surgical Clinic, Prof. Dr. Med. M. A. Kimbarowsky, Director.

1. Kenn, cited by Mondor, H.: *Diagnostics urgents: Abdomen*, ed. 2, Paris, Masson & Cie, 1933, vol. 1.

2. Gibe, cited by Mondor, H.: *Diagnostic surgents: Abdomen*, ed. 2, Paris, Masson & Cie, 1933, vol. 1.

the right half of the abdomen. There was tympanic resonance in the whole right half of the abdomen, the zone of the tympany passing to the external surface of the lumbar region. Hepatic dulness was maintained. The borders of the lungs and heart were normal. Six hours after injury a laparotomy was performed in the midline. Small multiple tears of the ascending colon and the transverse colon about the liver were detected, as well as multiple ruptures of the sero-muscular coat of the ascending colon. Some accumulation of blood in the lower part of the peritoneal cavity and in the Douglas pouch was noted. There was marked retroperitoneal emphysema. A retroperitoneal rupture of the ascending colon was suspected. The large intestine was mobilized. In the retroperitoneal space a hematoma of considerable size was detected. The posterior wall of the ascending colon was traumatized and was infiltrated with blood. A rupture 4 cm. in length was revealed in the retroperitoneal portion of the duodenum at the site of passage of the descending part of the duodenum into the lower, horizontal part. Resection of the mobilized part of the large intestine, followed by an end to side ileocolostomy, was performed. The duodenal tear was closed with a double line of sutures. Careful peritonization at the site of rupture was accomplished and the omentum was sutured to the line of peritoneal sutures. The abdominal wound was closed.

The postoperative course was aggravated by bilateral lobar pneumonia with an abscess of the right lung. On the sixteenth day, in spite of the absence of any evidence of infection in the peritoneal cavity and in the right lumbar region, a disruption of the wound in its lower half occurred, with evisceration of the intestinal loop, which had been well delimited from the free peritoneal cavity by adhesions. One day later a fistula of the transverse colon developed. There were increased symptoms of disease of the lungs; abscess and gangrene of the right lung were present. The patient died on the twenty-first day after injury.

Autopsy.—Myocardial degeneration and induration of the inferior lobe of the left lung (lobar pneumonia) were observed. The right lung was edematous and infiltrated. The upper part of the inferior lobe was occupied by the abscess cavity, the walls of which consisted of gangrenous tissue. There were multiple loose adhesions between loops of small intestine. An eviscerated loop of the ileum and a part of the colon were well delimited from the free peritoneal cavity. The duodenal suture was in good condition. In the region of suture of the parietal peritoneum an inflammatory infiltration without suppuration was noted. The anastomosis and the stump of the transverse colon were in good condition. Three centimeters above the anastomosis and 5 cm. from the stump on the anterior wall of the transverse colon a fistula 0.5 cm. in diameter was observed. Between the loop of the small intestine and the anterior peritoneal wall at the left a well encapsulated round abscess 1 cm. in diameter was seen. The subdiaphragmatic and the Douglas pouch showed no unusual conditions.

Attention must be drawn to the fact that, in spite of the presence of traumatic injuries of the large intestine along with the retroperitoneal duodenal rupture, peritoneal symptoms were not sharply marked; now and again they almost disappeared. As the condition of the patient was very poor and caused me to suspect a rupture of the hollow or parenchymatous organ, a laparotomy was done. Particular attention has been drawn to the symptom of extension of the zone of tympanic resonance to the right lumbar region as a result of the retroperitoneal

emphysema. The green spot on the parietal peritoneum, insisted on by Lafitte,³ was not observed. The extreme emphysema forced me to look for perforation in the colon and the duodenum retroperitoneally.

The case demonstrates the necessity of a careful investigation of the retroperitoneal region of the duodenum in the presence of retroperitoneal emphysema.

3. Lafitte, H.: *Arch. franço-belges de chir.* **34**:117 (Feb.) 1934.

MAGGOT THERAPY FOR HEMATOGENOUS OSTEOMYELITIS OF THE TIBIA

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WITH THE ASSISTANCE OF

DOROTHY JENSEN, A.B.

BOSTON

When Baer¹ announced in 1929 that he was using live blowfly maggots to treat osteomyelitis, there was a decided wave of interest throughout the United States. Many surgeons began using the method, and enthusiastic reports² appeared in the literature. After this preliminary wave of enthusiasm the use of maggots became more limited, but certain clinics have continued the practice. At present it is difficult to evaluate the method from the literature or to determine how widely it is used.

The purpose of this communication is to present in some detail a series of 29 cases in which hematogenous osteomyelitis of the tibia has been treated during the past seven years and which have been followed up to the time of writing. Most of the patients had been operated on by other surgeons, and treatment with maggots was begun after a period of antecedent treatment. Any additional operations were performed by me. In most instances the preliminary procedure was of the Orr³ type. The series lacked uniformity of operative treatment but by the same token was representative of various types of surgical technic and experience, so that the results are comparable with those which might be expected in private practice.

From the Osteomyelitis Clinic, the Surgical Research Laboratory and the Fifth (Harvard) Surgical Service of the Boston City Hospital.

Dr. Frederic J. Cotton originally suggested the use of maggots and was instrumental in obtaining technical assistance in producing them. Dr. Otto J. Hermann, chief of the orthopedic service, assisted in this work. Drs. A. R. Kimpton, R. C. Cochrane, J. H. Shortell, W. R. Morrison, C. C. Lund, J. H. Burnett, T. H. Peterson, R. H. Aldrich, L. R. Dretler, C. H. Bradford and P. W. Shannon, of the Boston City Hospital staff, referred cases observed in this report.

1. Baer, W. S., in discussion on Bitting, N. D.: Acute Osteomyelitis and Complications, *South. M. J.* **22**:580-583 (June) 1929.

2. Robinson, W.: Progress of Maggot Therapy, *Am. J. Surg.* **29**:67-71 (July) 1935.

3. Orr, H. W.: New Method of Treatment of Chronic Infections Involving Bone, *Nebraska M. J.* **8**:50-52 (Feb.) 1923.

The literature has grown so voluminous that it is impossible to review it here. The reader is referred to the bibliography compiled by Robinson.⁴

OPERATIVE PROCEDURE

The preliminary operative treatment of the subacute condition was essentially that described by Orr.³ In some instances several operations had been performed before maggot treatment was begun. Patients with chronic osteomyelitis who came directly to me were usually treated with maggots for from two to four weeks before any operation was performed. A few of the lesions healed without operative intervention. When operation proved necessary, all infected bone and scar tissue was removed, a base of viable bone being left. The cavity was packed with petrolatum gauze, and a cast was applied. In all the cases of bone abscess (Brodie⁵) described here the lesion had been opened wide and packed with petrolatum gauze by another surgeon before the patient was referred to me for maggot treatment.

METHODS

The production and sterilization of maggots have been described so carefully by several writers⁶ that no mention need be made of this process. All the methods are essentially the same, but the latest technic of Robinson^{6c} has proved the simplest and most satisfactory.

Maggot Therapy.—Approximately one week after the operation in cases of chronic osteomyelitis or four weeks or more in cases of acute disease the petrolatum gauze packing is removed. Any accumulation of pus is sponged out, and the bleeding is controlled by pressure. In order to establish maggots promptly, the wound is rendered alkaline by irrigation with a 0.25 per cent suspension of calcium carbonate.⁷ After irrigation the wound is gently sponged dry, and enough maggots are inserted to cover its surface. The exact number in any given case can be determined only by experience and experiment. The skin is protected with some waterproof material in order to prevent its being digested by the enzymes in the excreta of the maggots. After the implantation the depths of the wound are packed lightly with fluffed gauze, and the whole is covered

4. Robinson, W.: Literature Relating to the Use of Maggots in the Treatment of Suppurative Infections, Bulletin 310, United States Department of Agriculture, Bureau of Entomology, 1934.

5. Brodie, B.: Lecture on Abscess of the Tibia, London M. Gaz. 36:1399-1403, 1845.

6. (a) Child, F. S., and Roberts, E. F.: The Treatment of Chronic Osteomyelitis with Live Maggots, New York State J. Med. 31:937-943 (Aug. 1) 1931. (b) Livingston, S. K.: Maggots in the Treatment of Chronic Osteomyelitis, Infected Wounds and Compound Fractures, Surg., Gynec. & Obst. 54:702-706 (April) 1932. (c) Robinson, W.: Improved Methods in the Culture of Sterile Maggots for Surgical Use, J. Lab. & Clin. Med. 20:77-85 (Oct.) 1934.

7. Stewart, M. A.: A New Treatment of Osteomyelitis, Surg., Gynec. & Obst. 58:155-165 (Feb.) 1934.

with gauze and cellulocotton pads. This type of dressing is much simpler than any of the cages which have been recommended and has the great advantage of keeping the wound from becoming filled with pools of pus in which the maggots will drown.

Contrary to general practice, the dressings are usually changed daily. This keeps the skin in good condition and adds materially to the comfort of the patient. It is possible to remove some of the maggots when they are obviously crowding the wound and causing pain or to replace them if they have failed to survive.

Clinical Course.—One may expect the wound to put forth healthy granulation tissue within from two to four weeks after the beginning of the treatment. Small chips and lumps of cancellous bone make their appearance during this period and can be lifted out with forceps. Occasionally the edges of the osseous defect and small islands of firmly attached bone will fail to granulate. Such areas are insensitive and can be removed with rongeurs or a gouge, without anesthesia. After their removal, bleeding is stopped by pressure, and treatment with maggots can be continued at once or on the following day.

If during the course of treatment the wound fails to make reasonable progress, roentgenograms will often reveal some deep area of involvement which has been overlooked at operation. Insertion of a probe in a suggestive depression in the wound while the films are being taken often serves to point out the offending bone. Patients with such involvement should not be reoperated on at once if the wound is making satisfactory progress. Considerable judgment is required to determine the best course to pursue. Many such apparent sequestrums revascularize and are incorporated into the new bone. Others become more sharply demarcated in time and can be removed mechanically without anesthesia.

Maggots need not be left in the wound until complete epithelization has occurred, but the question of the proper moment to discontinue their use is at times difficult to decide. In general, the best criteria are a healthy looking wound and a roentgenogram showing no abnormality. It is my custom to remove maggots at this stage and substitute urea crystals⁸ or dry dextrose. Some wounds regress after this change, and it is necessary to return to treatment with maggots. Others show steady improvement, and the skin begins to grow in from the edges; in such the lesions should be prepared for skin grafts. This procedure not only hastens closure but produces skin over the affected area which is better able to withstand possible future injury.

Patients are allowed to sit up as a routine as long as they remain afebrile. Crutches are issued as soon as the wound becomes well covered with granulations, and their use is continued until complete closure has occurred. When involvement of the legs is bilateral, walking is permitted as soon as the wound on one leg is closed. Healing of the skin sometimes has been delayed by allowing the patient to hold the leg in a

8. Holder, H. G., and MacKay, E. M.: The Use of Urea in the Treatment of Infected Wounds, J. A. M. A. 108: 1167-1169 (April 3) 1937.

dependent position; this results in venous congestion. The delay required for correct healing is more than offset by the advantage of early return to work. Patients are kept in the hospital only until it becomes probable that no further operations on the bone will be necessary. They are then sent home with directions to return to the clinic for treatment.

In some cases treatment with maggots was not begun until after the patient was discharged from the hospital. It was found feasible to use the treatment for ambulatory patients, with three dressings per week. Such patients were occasionally readmitted to the hospital for sequestrectomy or skin grafts.

After closure has occurred the patient is told to return at intervals of from one to three months for clinical and roentgen examination. The intervals are gradually lengthened, but each patient is seen every six months.

Death of Maggots in Wounds.—In all of his papers Baer referred to the phenomenon of death and dissolution of maggots, which occurred in each case toward the end of the healing process. He regarded this as due to acquired immunity of the patient to maggots. Livingston and Prince⁹ explained it as being due to the development of a higher p_H and to the production of their "active principle." During the present investigation the dying out of maggots has never been observed. Late in the treatment the maggots do not grow rapidly, and many doubtless die of inanition, but they have never been seen to dissolve in the wound. That the patient does not acquire immunity to maggots has been amply demonstrated in numerous cases in which treatment was stopped for periods varying from one week to almost a year.¹⁰ On resumption of treatment there was no evidence of inability of the maggots to survive. Several patients have had multiple lesions which healed at different times, yet the last wound in each case continued to support maggots as long as they were used. A few patients have returned with localized infections in the overlying soft parts. These have often been treated with maggots, and it has never been found difficult to establish or maintain the larvae. It would seem, therefore, that the death of maggots is probably caused by starvation, escape from the wound or low viability of the culture.

RESULTS

The results of this study are given in table 1 and summarized in table 2. The 29 cases are grouped under appropriate headings and

9 Livingston, S. K., and Prince, L. H.: *The Treatment of Chronic Osteomyelitis with Special Reference to the Use of the Maggot Active Principle*, J. A. M. A. **98**:1143-1149 (April 2) 1932.

10 Maddock, S., and Jensen, D.: *The Treatment of Septic Compound Fractures of the Tibia with Maggots*, New England J. Med. **217**:123-129 (July 22) 1937.

numbered in each group according to the time at which maggot therapy was started. The series seems to be divisible naturally into three categories, the first including cases of subacute osteomyelitis; the second, cases of chronic osteomyelitis, and the third, cases of abscess of the bone (Brodie⁵). There was no case of true acute osteomyelitis in the series, since treatment with maggots was not started until the patient had passed through the critical febrile phase of the illness.

TABLE 1.—*Results of Maggot Treatment*

Case	Age	Date of Onset	Premaggot Operation	Maggot Therapy Started	Maggot Therapy Stopped	Discharge from Hospital	Result	
Subacute Hematogenous Osteomyelitis								
1	14	2/14/31	8/ 7/31	8/21/31	11/ 8/31 12/25/31	12/25/31	Closed.....	11/19/31 R 2/16/32 L
2	9	8/12/31	8/21/31	8/29/31	9/25/31	11/ 6/31	Closed.....	8/12/32
3	7	8/29/31	9/ 2/31	2/10/32	4/ 6/32	5/ 5/32	Closed.....	12/12/32
4	5	8/ 9/31	1/21/32	2/14/32	3/13/32	4/28/32	Closed.....	10/15/32
5	11	5/25/32	6/12/32	6/29/32	7/31/32	2/23/33	Amputation..	11/11/32
6	16	5/25/32	6/ 3/32	6/12/32	9/21/32	2/12/33	Amputation..	2/12/33
7	14	12/10/32	4/18/33	5/16/33	10/14/33	7/ 3/32	Closed.....	10/16/33
8	14	8/30/32	11/15/32	2/ 3/33	2/ 8/34	4/14/33	Closed.....	5/ 1/34
9	13	2/12/34	3/18/34	4/ 2/34	9/ 4/34	5/28/34	Closed.....	1/11/35
10	14	7/31/34	8/ 4/34	8/27/34	11/12/35	10/31/34	Closed.....	1/25/36
11	12	2/17/35	2/18/35	3/26/35	2/ 7/36	12/ 5/35	Closed.....	2/23/37
12	8	8/ 3/34	8/ 4/34	4/ 9/35	10/23/35	10/ 5/35	Closed.....	1/22/36
13	14	10/15/35	10/18/35	12/11/35	2/22/36	11/22/35	Closed.....	12/14/36
14	9	10/10/35	10/14/35	1/ 2/36	2/22/36	12/15/35	Closed.....	6/28/36
15	9	8/ 9/35	11/16/35	1/ 7/36	3/ 2/36	12/18/35	Closed.....	5/12/37
16	11	10/12/35	10/20/35	1/ 7/36	2/22/36	4/19/36	Closed.....	4/19/36
17	15	7/31/36	11/24/36	1/ 5/37	3/10/37	6/ 3/37	Closed.....	3/17/37 L 6/ 1/37 R
Chronic Hematogenous Osteomyelitis								
18	53	1889	1/14/31	2/ 6/31	5/30/31	6/ 4/31	Closed.....	3/12/35
19	30	1912		11/26/32	12/29/32	6/12/33	Closed.....	10/ 1/33
20	55	1912		12/19/32	1/21/33	4/26/33	Lost	
21	19	1929	4/11/33	5/ 6/33	6/26/33	8/16/33	Lost	
22	49	1895	6/14/34	6/18/34	7/20/34	8/18/34	Closed.....	9/ 2/34
23	10	1933	5/24/33	12/ 9/35	1/ 2/36	6/21/33	Closed.....	2/20/36
24	51	1900	11/29/35	1/ 2/36	2/12/36	12/28/35	Closed.....	9/25/36
Brodie's Abscess								
25	12	?	8/ 3/31	8/13/31	9/ 5/31	8/27/31	Closed.....	6/ 2/32
26	51	?	2/ 8/34	2/17/34	4/14/34	4/ 1/34	Treatment	
27	6	10/20/33	5/ 7/34	7/ 8/34	10/ 2/34	7/ 6/34	Closed.....	1/ 5/35
28	43	?	10/12/34	1/21/35	6/10/35	10/31/34	Closed.....	8/ 7/35
29	40	1924	1/ 9/36	1/16/36	2/12/36	2/22/36	Closed.....	2/23/36

Group 1 (Subacute Osteomyelitis).—There were 17 cases in this group; in 2 of these there were bilateral lesions. Of the 19 tibias involved by osteomyelitis, 2 required amputation, and at the time of writing the remaining 17 lesions had been closed for periods varying from one month to five and one-half years. An average period of two years had elapsed since final closure. The ages of the patients varied from 5 to 16 years. The average age at onset was 11.6 years. There were 4 girls and 11 boys. Trauma was noted as an exciting cause for localization in 10 cases. Previous infection was recognized in 8 cases. Positive blood culture was obtained in 15 cases and obtained repeatedly in 5. The organism recovered from the bone and from the blood stream was

Staphylococcus aureus in every case. In 6 cases the entire shaft was involved, with complete sequestration in 2 (cases 4 and 10). In 9 instances the lower third and in 4 the upper third of the tibia was affected. Skin grafts were used in 5 cases to hasten final closure.

Untoward Results: Ankylosis occurred in the ankle in 4 cases and in the knee in 1. In all the cases there was primary involvement of the joint, so that such an end result was anticipated. The patient in case 3, who had involvement of the knee, was discharged to a convalescent home without medical supervision, and the knee became ankylosed in about 40 degrees' flexion. An operation for the correction of this deformity is contemplated at an early date, since at the time of writing closure had persisted for over five years.

TABLE 2.—*Classification of Results According to Type of Lesion*

Type of Lesion	No.	Closed	Under Treatment	Limb Amputated	Lost	% Closed	Period from Onset to Institution of Maggot Treatment	Period of Maggot Treatment	Period from Treatment to Closure	Total Period of Illness	Time in Hospital	Time Since Closure
Subacute osteomyelitis	19	17	0	2	0	89	106 days	106 days	205 days	417 days	169 days	2 years
Chronic osteomyelitis	7	5	0	0	2*	100	23 years	48 days	303 days	24† years	182 days	2.07 years
Abscess of bone	5	4	1*	0	0	100	5 years	66 days	79 days	?	80 days	2.87 years
Average.....						92						

* Omitted in calculating average figures.

† Time from pre-maggot operation to closure.

Amputations: The cases in which amputation was performed are worthy of special consideration. The patient in case 5 was treated at another hospital, so that daily care under my supervision was impossible. The entire shaft of the tibia was involved. So many abscesses developed in the soft parts that after a few weeks almost one third of the leg was destroyed. Because of the difficulty of treating a patient in another hospital, maggot treatment was abandoned after thirty-two days. The leg was amputated about four months later.

The patient in case 6 was a boy with a history of polycythaemia vera of three years' duration. The osseous lesion involved the upper third of the tibia. Operation was done on June 3, 1932. Treatment was begun on June 12 and was continued until September 21. During this period the wound showed moderate improvement. On June 16 acute phlebitis of the popliteal vein developed. On August 18 an abscess of the posterior wall of the chest was found, which subsequently proved to be secondary to osteomyelitis of the seventh rib. Because of the poor general condition of the patient amputation at the level of the mid thigh

was performed on September 27. Reamputation was necessary on December 15, and the patient was discharged from the hospital five months later.

Group 2 (Chronic Osteomyelitis).—In the 7 cases in this group there was a history of osteomyelitis of from twelve to forty-two years' duration. Four of the patients had shown closure of the lesion for long periods but entered the hospital because of local recurrences; the lesions of the other 3 had never closed. Table 2 shows that actual treatment with maggots was of fairly short duration (an average of forty-eight days). The length of the average interval, three hundred and ninety-three days, between the discontinuance of maggot therapy and final closure of the lesion was caused by a delay which occurred in a single case (case 18). The patient in this case left my care after one year and was reoperated on by another surgeon. There was no improvement, and the patient returned in about a year for further treatment. The wound finally closed after a total of four years' treatment. The average length of time from the discontinuance of treatment with maggots to closure of the lesions for the other patients in this group was one hundred and forty-six days. The period of hospitalization given refers only to the stay during which maggots were used. At the time of writing closure had persisted for an average period of two and seven hundredths years.

Lost Patients: Both the patients recorded as lost had closed lesions, but credit cannot be taken for the cures, as is indicated by the following protocols:

The patient in case 21 was transferred to a hospital for chronic diseases at a time when the leg seemed to be healing satisfactorily. During hospitalization a resection of the middle two thirds of the tibia was performed. At the time of writing a roentgenogram showed fusion of the upper and the lower end of the tibia with the fibula, which had greatly hypertrophied. The residual bone appeared fairly normal, and the wound was closed.

The other patient (case 20) fell into other hands and was operated on twice after maggot treatment was stopped. He left the hospital before closure was attained. He returned a year later. He was reoperated on, and skin was grafted into the lesion. Complete closure resulted.

Group 3 (Abscess of Bone [Brodie]).—The exact time of onset of the condition could not be determined in all cases of this group. In 2 (cases 27 and 29) it was known because of the occurrence of multiple foci; in the other 3 the lesions were "silent" at the onset. At the time of writing 1 patient was still under treatment; the other 4 had had closed lesions for an average period of two and nine-tenths years.

The patient still under treatment (case 26) had alopecia totalis and myxedema. In 1935 she had eczema around the wound and in other portions of the body. Treatment was greatly interfered with by these

complications. An operation performed on Sept. 13, 1937, revealed marked overgrowth of subperiosteal bone, with bare, eburnated necrotic bone in the depths of the wound. This was removed, and maggot treatment was begun on October 1. The lesion closed on October 23.

The entire series, then, comprises 29 cases, with involvement of 31 tibias. Two lesions necessitated amputation; the further course of 2 is not known; 1 (not included in averages) was under treatment when this report was made, and the remaining 26 lesions were closed. Exclusion of the lesions lost from observation and those under treatment leaves 92 per cent closed. The lesions in the 2 cases recorded as lost were also closed, but closure was preceded by additional operations. Closure had persisted for an average period of more than two years.

Osseous lesions have not recurred in any of the patients, although several have had severe blows over the site of the former lesion, causing abrasions of the scar. Such lesions in scars have always responded to conservative measures and have never required operation.

Roentgen Findings.—Final roentgenograms were obtained during May and June 1937. These were examined by a roentgenologist, who concluded that all except one indicated healed lesions. The exception (in case 28) showed two discrete abscesses of the upper end of the tibia, and at operation only one of these had been opened. The patient was told of the lesions but preferred to continue working until they caused trouble. The roentgenographic appearance of the bones in the other cases varied from almost perfect anatomic restoration of the trabecular architecture to extensive enlargement of the shafts, caused by overgrowth of involucrum.

COMMENT

The crux of the treatment of hematogenous osteomyelitis lies in the question of whether the lesion is actually healed or is merely covered with integument under which infection is smouldering. In this communication considerable stress has been placed on the end results, because no publications have shown the results of similar treatment. It has become customary in the literature to refer to the status of lesions as healed, improved or unimproved. I have tried to use the less misleading terms "closed" and "under treatment." The word "healed" is meaningless unless the patient has been followed for thirty or forty years. The term "improved" is equally inappropriate since, as Lewis¹¹ pointed out, "improvement usually means a discharging sinus or unhealed wound and indicates that surgery has not attained its aim."

The end results given by various authors in cases of osteomyelitis of all bones were summarized by Wilensky¹² in tabular form. The

11. Lewis, D.: *Acute Osteomyelitis*, J. A. M. A. **92**:783-786 (March 9) 1929.

12. Wilensky, A. O.: *Osteomyelitis*, New York, The Macmillan Company, 1934.

figures showed wide variation in the percentage of cases in which cure was recorded. Investigation of the original articles showed that the reported results were based largely on the status of the lesion at the time of the patient's discharge from the hospital, which, as Farr¹³ remarked, depends on the degree of optimism of the house surgeon. My experience has been that many promising-looking lesions regress and persist for long periods after the patient leaves the hospital and that a consistent policy of after-care is necessary for really good results.

The great advantage in the use of maggots seems to lie in the high percentage of closed lesions and in the relative scarcity of recurrences. This is doubtless due to the ability of the larvae to uncover hidden sequestrums and to seek out small abscesses which might otherwise become included in the new bone. This characteristic of maggots assumes more importance since the recent demonstration by Buchman¹⁴ that treatment with staphylococcus antitoxin and toxoid does not prevent recurrences or materially influence the progress of the local lesion. My own experience in this field, although not as extensive as that of Buchman,¹⁴ tends to confirm his conclusions in every respect. The other advantages of treatment with maggots have been discussed fully.¹⁵

In criticism of maggot therapy it has been argued that the method is time consuming, expensive and painful. As shown in table 2, actual treatment with maggots occupies only 25 per cent of the entire period of disability in cases in which the condition is subacute, and in those in which it is chronic, a mere fraction of this total. The expense is not great when one considers the amount of time which is ultimately saved. A certain number of patients complain of pain, but with the use of sedatives, anesthetic ointments and frequent dressings this is never a serious drawback. Patients with long-standing wounds are willing to submit to discomfort if they can be given hope of ultimate cures.

I do not think that maggot therapy is indicated in all cases of osteomyelitis. The treatment described and practiced by Orr³ should certainly be the ideal procedure in every case in which the condition is subacute. Only when the patient fails to make reasonable progress clinically is it necessary to consider the use of maggots. For chronic

13. Farr, C. E.: Acute Osteomyelitis in Children, *Ann. Surg.* **83**:686-692 (May) 1926.

14. Buchman, J.: The Use of Staphylococcus Toxoid in the Treatment of Chronic Osteomyelitis, *J. A. M. A.* **108**:1151-1156 (April 3) 1937.

15. Baer, W. S.: The Treatment of Chronic Osteomyelitis with the Maggot (Larva of the Blowfly), *J. Bone & Joint Surg.* **13**:438-475 (July) 1931. Robinson, W., and Norwood, V. H.: The Role of Surgical Maggots in the Disinfection of Osteomyelitis and Other Infected Wounds, *ibid.* **15**:409-412 (April) 1933. Buchman, J., and Blair, J. E.: Maggots and Their Use in the Treatment of Chronic Osteomyelitis, *Surg., Gynec. & Obst.* **55**:177-190 (Aug.) 1932. Maddock and Jensen.¹⁰

osteomyelitis their usefulness is probably much greater. It is doubtful that anything but maggot therapy could have produced closure of some of the chronic lesions in this series. Brodie's abscess was treated with maggots because in my cases it had been opened and packed by other surgeons. This lesion is more properly managed by conservative methods, such as primary closure¹⁶ and irrigation for a short period, with secondary closure.¹⁷

It is natural to wonder whether maggot therapy for osteomyelitis is a medical fad or a significant contribution to science. After seven years of experience and many trials of various substitutes I still feel that the condition can be treated profitably with maggots and that no lesion should be given up as hopeless until maggot therapy has been tried.

SUMMARY

A series of 31 lesions in 29 cases of hematogenous osteomyelitis of the tibia treated with maggots is presented. The patients were followed up to the time of writing. Twenty-six of the lesions were closed, 1 still required treatment, 2 had necessitated amputation and 2 were lost. The management of wounds under maggot treatment is described. The chief objections to treatment with maggots are the time consumed, the expense and the pain. It is pointed out that none of these objections is particularly serious. The advantages of maggots are: rapid débridement of necrotic material, discovery of hidden sequestrums and pockets of pus, stimulation of granulations, continuous treatment, shortening of hospitalization and early rehabilitation of the patient. Subacute osteomyelitis of the tibia should rarely become chronic, because of the easy accessibility of this bone.

16. Brickner, W. M.: The Treatment of Chronic Bone Abscesses by Simple Evacuation Through a Small Drill Hole, *J. Bone & Joint Surg.* 5:492-500 (July) 1923.

17. Wilensky,¹² p. 231.

END RESULTS OF TUBERCULOUS CYSTITIS

REPORT OF CASES

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The problem of renal tuberculosis has received exhaustive attention for many years. It is now generally recognized that the condition is a local manifestation of a general disease, and treatment is executed with that fact in mind. Most clinical discussions begin with mention of frequency of urination as the most common chief complaint and end by saying that the vesical lesions usually heal in from six months to a year after removal of the offending kidney. However, the failure of the urinary bladder to resume a normal condition after removal of all tuberculous foci in the urinary tract is not uncommon. French writers have called attention to the necessary activity of the bladder as a possible reason for failure of the lesions to heal. For other parts of the body rest is the best method of treatment, but for the bladder rest is impossible. The change in the vesical wall may be multiple ulcers causing a painful frequency of urination or the condition may progress to produce the well known contracted and sclerotic bladder wall with an extreme reduction in capacity. The endless methods of treatment directed at the relief of this distressing condition by their very number attest to frequent failure.

With tuberculous cystitis, as with other conditions involving destruction of the normal function of the bladder, the upper portion of the urinary tract is endangered. The process may so involve the intramural portion of the ureter from the single kidney as to result in hydronephrosis and eventual destruction of the kidney. Before this occurs the capacity of the bladder may be so reduced as to cause a frequency of urination not dissimilar to incontinence. The urgent necessity of relief for both of these conditions is apparent.

Nephrostomy, cystostomy, ureterostomy and ureteral transplantation to the rectum have all been used as palliative procedures. Hinman¹ reported 4 cases in which he made ureteral transplants to the rectum because of extreme frequency of urination or a beginning dilatation in the remaining, nontuberculous kidney. In 2 of his cases he did pre-

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1. Hinman, F.: Surgical Treatment of Lower Tract Tuberculosis, Genital and Vesical, *J. Urol.* 20:521-538, 1928.

liminary nephrostomies. At the time of his report (1928) 1 patient was still living two years after the operation. Hinman's paper recorded the most extensive experience I was able to find in the literature dealing with the complete destruction of function by persisting tuberculous cystitis.

As an example of the possibly destructive nature of tuberculous cystitis I wish to report 2 cases, in which there were different lesions and different operations.

REPORT OF CASES

CASE 1.—W. G. H., a man aged 22, was admitted to the hospital on May 7, 1936, complaining of frequency of urination which began in 1931. Since that time



Fig. 1.—Dilated pelvis and ureter.

the condition had become progressively worse until the time of his admission, when he was urinating every hour day and night. In January 1936 he was forced to wear a urinal. He had noticed hematuria and pyuria on many occasions.

Physical examination showed a young man in a fair state of nutrition. His weight was 128 pounds (58.1 Kg.). The lungs were clear, and the heart was normal. The right kidney was palpable and tender. The prostate was somewhat enlarged, nodular and tender. The external genitalia were normal.

The urine contained much pus and many red blood cells. Studies of the blood showed normal conditions. The nonprotein nitrogen content was 31, and the excretion of phenolsulfonphthalein was 50 per cent in two hours. A roentgenogram of the chest showed no active disease.

Cystoscopic examination with the patient under spinal anesthesia revealed a contracted bladder with much edema and many tuberculous ulcers, most marked around the right orifice. Excretory urograms demonstrated satisfactory filling in the left kidney in seven minutes (fig. 1). The pelvis, calices and ureter were

dilated to three times the normal size, and the ureteral dilatation extended down to the bladder wall. No dye appeared in the right kidney in any of the plates. Staining of urine from the bladder showed tubercle bacilli. Because of the apparently functionless kidney on the right and the dilatation of the left ureter, a nephrostomy was done on the left side on May 21. Two months later a nephrectomy was performed on the right side. The kidney showed tuberculous pyonephrosis. Guinea pigs inoculated on two occasions with urine from the left kidney showed no evidence of tuberculosis. Figure 2 shows an excretory urogram taken on July 9. Both the pelvis and the ureter were well filled and showed that improvement had taken place since the introduction of the nephrostomy tube. The patient emptied his bladder only once a day.

In April 1937, one year after the nephrostomy, the patient returned for a check-up. A pyeloureterogram (left side) taken after injection of the nephrostomy tube showed the pelvis and calices to be fairly normal, but the ureter remained dilated and tortuous (fig. 3).

Not only has this patient been made much more comfortable than he has been in several years, but a destructive process in the left kidney has been arrested.

CASE 2.—W. G. H., a man aged 54, was first admitted to the hospital on Dec. 6, 1931. The chief complaint was of dysuria and of frequency of urination, with voiding every ten minutes day and night. He had had the right kidney removed in 1914 because of tuberculosis. At the time of this operation he was having frequency of urination and dysuria. The nephrectomy wound drained for three years before healing. After this operation epididymitis developed, with draining sinuses in the scrotum.

Physical examination showed a well developed, well nourished man weighing 162 pounds (73.5 Kg.). The lungs were clear. The nephrectomy scar on the right side was well healed. A bilateral inguinal hernia was present. The epididymes were indurated, and the scrotum showed healed scars marking the site of the draining sinuses.

The urine contained many white blood cells and red blood cells. Twenty-four hour specimens of urine showed no tubercle bacilli. Cystoscopic examination showed a definitely contracted bladder. The left ureter could not be catheterized. The capacity of the bladder was 30 cc. (under spinal anesthesia). Excretory urograms demonstrated satisfactory filling of the left renal pelvis in five minutes. The pelvis and calices were apparently normal, and nothing was suggestive of tuberculosis (fig. 4). Irrigations with phenol were done. This produced some improvement in the cystitis, but the bladder could not be distended sufficiently for catheterization of the left ureter. Owing to the contraction of the bladder, which made this organ absolutely useless, the left ureter was transplanted into the sigmoid on April 14. The postoperative course was satisfactory. At the time of his discharge the patient was able to hold the urine in the bowel for three to six hours.

Excretory urograms taken as a check-up showed a normal left kidney (fig. 5A). Excretory urograms taken three years later, in 1935 (fig. 5B), showed the upper and lower calices to be dilated to twice the normal size. The middle calyx was normal. The ureter was dilated to twice the normal size. The patient returned to this hospital on Sept. 18, 1937, five and a half years after the operation, for a check-up. Figure 5C is the excretory urogram taken at this time. He was in excellent general physical condition. He stated that he was emptying his bowels about every four hours. His weight was 185 pounds (83.9 Kg.).



Fig. 2.—Excretory urogram showing reduction in the size of the pelvis after a nephrostomy.



Fig. 3.—Pyeloureterogram taken after injection of the nephrostomy tube. The size of the pelvis is approximately normal. The ureter remains dilated.



Fig. 4.—Excretory urogram taken before a ureteral transplantation.

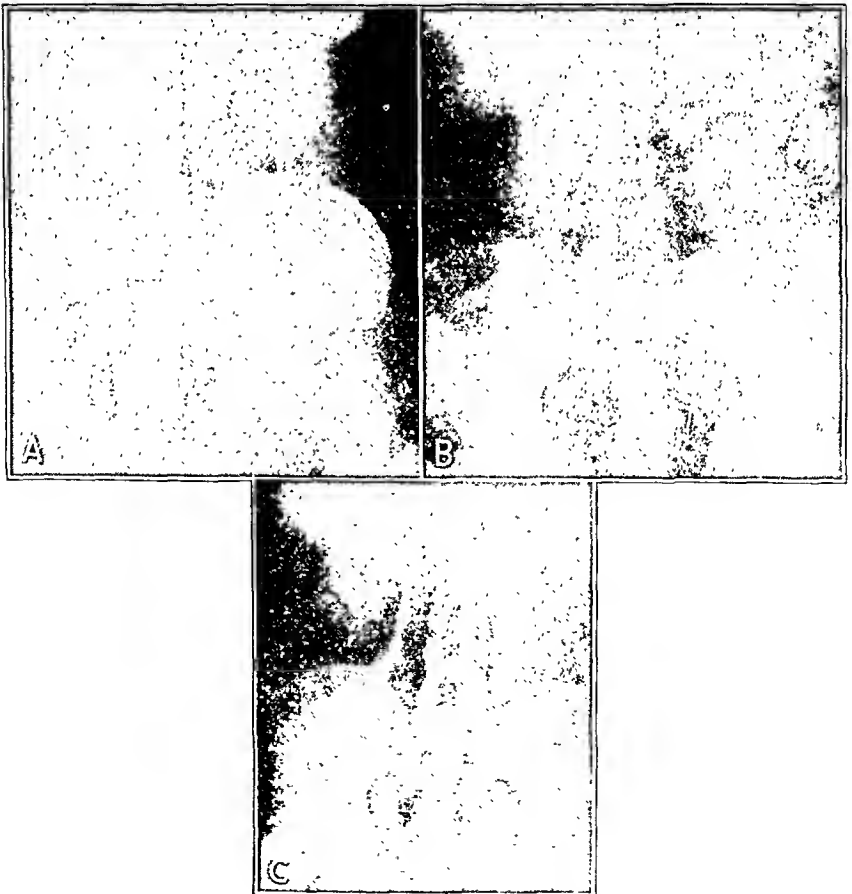


Fig. 5.—Results of ureteral transplantation: *A*, excretory urogram taken two months after transplantation; *B*, excretory urogram taken three years after transplantation; *C*, excretory urogram taken five and one-half years after transplantation.

This patient's bladder was so destroyed by fibrous tissue that instead of being an organ of convenience it had become a source of constant pain and discomfort, resulting in incontinence. Even though his remaining kidney was normal, his life was unbearable. What eventually would have happened to this kidney it is impossible to say, but the irreparable damage to the bladder made some procedure necessary.

COMMENT

These 2 cases demonstrate what occasionally may occur as the end result of tuberculous cystitis, namely: (1) destruction of an uninfected kidney by ureteral obstruction and (2) total loss of vesical function as a result of sclerosis and of destruction by fibrous tissue.

CYSTS OF EXTERNAL SEMILUNAR CARTILAGE

REPORT OF THREE CASES

SAMUEL KLEINBERG, M.D.

NEW YORK

Although the literature contains records of a fairly large number of cysts of the semilunar cartilages, Bennett and Shaw having recently collected 163 cases, only a few surgeons have treated the condition in more than 1 or 2 cases. I reported a cyst of the external meniscus in 1927 and did not see another until 1937. Compared with other derangements of the knee, such as torn and displaced semilunar cartilages, cysts of either cartilage are rare. Nor is it likely that many are missed or undiagnosed, because the symptoms are noticeable, and the lesion sooner or later reaches conspicuous proportions and interferes with function of the knee joint.

The symptoms of a cyst of the external semilunar cartilage are swelling, pain and variable disability. Tumefaction is the most important symptom. In the early stage the swelling is small and may be indistinguishable from the adjacent soft tissues. By the time a physician is consulted, however, the mass is visible and palpable. It is located in the interval between the tibia and the femur, at the joint line between the lateral ligament and the infrapatellar fat pad, but is distinct from both. The mass varies in size from that of a small hazelnut to that of a pigeon's egg. It is elastic, sometimes fluctuant and usually slightly sensitive to pressure. On complete extension of the knee the swelling diminishes or may even disappear by recession into the joint space, while on flexion it becomes prominent. The mass is firmly attached to the deep tissues but not to the overlying skin and subcutaneous tissues. Though there is some local sensitiveness, there is no evidence of inflammation. The swelling is readily palpated, but its limits are not sharply defined.

The pain is mild to moderate and is referred to the region of the tumefaction. It may radiate up the thigh or down the leg. Exercise increases the pain, and rest relieves it. With the majority of patients the onset of pain is insidious and seemingly is not initiated by any definite cause, such as trauma or excessive use. In a minority of cases the symptoms appear after an injury. The pain sometimes comes in attacks, being completely absent in the intervals. Finally, however, it becomes constant and fairly severe. In the early stages, when the mass is small, it does not cause any pressure on the surrounding tissues

nor does it interfere with the free mobility of the tibia on the femur; hence it does not cause discomfort. As the mass enlarges, however, it encroaches and presses on the joint capsule and the cartilage, causing pain.

The degree of disablement is variable. Most patients are able to walk as much as they please, noticing difficulty only when they first arise from the sitting position or when they first begin to walk. During attacks of moderate pain the patient may limit his activity, but he is never compelled to stop work. For sensitive persons the presence of a mass in the knee and the moderate discomfort create a physical and especially a psychic hazard which reduces activity. In an occasional case the cystic mass, which is perhaps loosely attached to the capsule, moves in and out of the joint, and the patient is aware of it; there may even be mild temporary locking of the knee. Actually, flexion and extension of the knee, both active and passive, are free. As time passes, the swelling, pain and disablement increase. The patient tires easily and may notice a continuous ache in the knee. At this stage he seeks medical aid and usually submits to an operation. I have had no experience with a patient who had harbored a meniscal cyst for many years. As this lesion occurs in young adults, who are not as hesitant about being operated on as older persons often are, and as the surgeon can assure complete relief on removal of the cyst and cartilage, one may reasonably assume that the lesion is always subjected to surgical treatment.

ETIOLOGY

Bennett and Shaw stated that the average age of the patients in 73 cases of cyst of the semilunar cartilage was 29.6 years. In my group of 4 cases, 3 presented in this communication and 1 previously reported, the average age was 28 years. Males are more frequently affected than females. These facts have led some surgeons to believe that this lesion is of traumatic origin. It is also true that there is a history of injury, sometimes rather vague, in about half the cases. Theoretically it is certainly conceivable that an injury to the front of the cartilage, damaging also the capsule, might result in a hematoma which might undergo cystic degeneration. The cyst or cysts, being loosely encapsulated, become enlarged, interfere with the local circulation and cause further cystic degeneration. A vicious circle is established, and the result is a cystic mass of the meniscocapsular tissues. Yet it is difficult to set aside the fact that there are no cysts in the hundreds of injured and dislocated menisci which physicians see and remove. Dr. H. L. Jaffe, pathologist at the Hospital for Joint Diseases, in discussing this problem with me, stated that he has at times seen microscopic cysts in the torn cartilages which I have sent to his laboratory. Clinically, however, I surely do not see any gross

multilocular encapsulated cysts in the removed menisci ruptured and dislocated by injury. It is worth recalling too that while the internal meniscus is damaged nine times more frequently than is the external meniscus, cysts occur much more often in the latter than in the former. It has been suggested that an injury may cause pinching off of a bit of synovial tissue, which, becoming encapsulated, gradually forms a cystic mass. This theory seems plausible because the cells lining the cysts and those lining the synovial tissue are histologically analogous. The specificity of the lesion and its location lead me to believe that it is caused by a metabolic disturbance in the cartilage, initiated by trauma or some unknown factor, as a result of which the cartilage cells necrose. Thus are formed defects which coalesce into cysts.

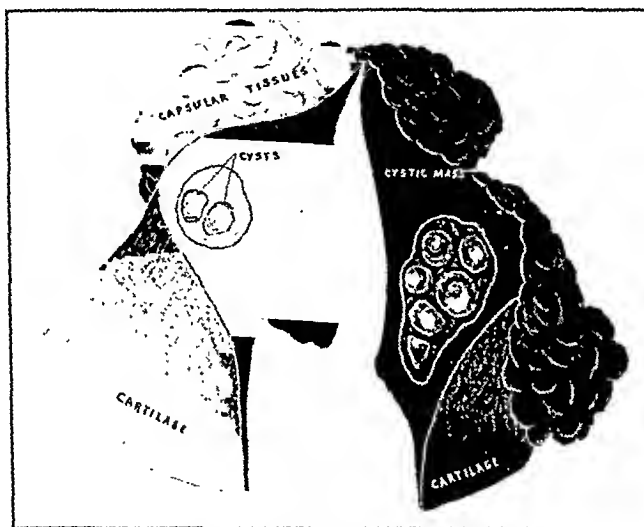


Fig. 1 (case 1).—Schematic drawing of the sectioned specimen. Multiple cysts of unequal size, encapsulated in the meniscocapsular tissues.

PATHOLOGIC PICTURE

The lesion under consideration consists of a multilocular cystic mass situated at the anterior border of the anterior or middle third of either the external or the internal meniscus. Parenthetically, it should be noted as a point against the theory of a simple traumatic cause that although the posterior third of the meniscus is often injured a cyst is never seen in that segment of the cartilage. The cystic mass (fig. 1) is enclosed in loose connective tissue and lies in the meniscocapsular tissues. The cystic mass is actually in and part of the peripheral portion of the cartilage. This location at and in the meniscocapsular junction makes it difficult to determine whether the cysts arise primarily in the cartilage and extend into the fibrous capsule, or whether

they form first in the capsulosynovial tissue and secondarily invade the cartilage. There are usually many cysts, some small, others large, filled with mucinous, glairy material. There is a limiting membrane, but this is loose, vascular and poorly defined.

The microscopic section shows a multilocular cystic area lying between and united to the cartilage and the capsule. A cross section (fig. 2) may conveniently be divided into an avascular segment (*A*),

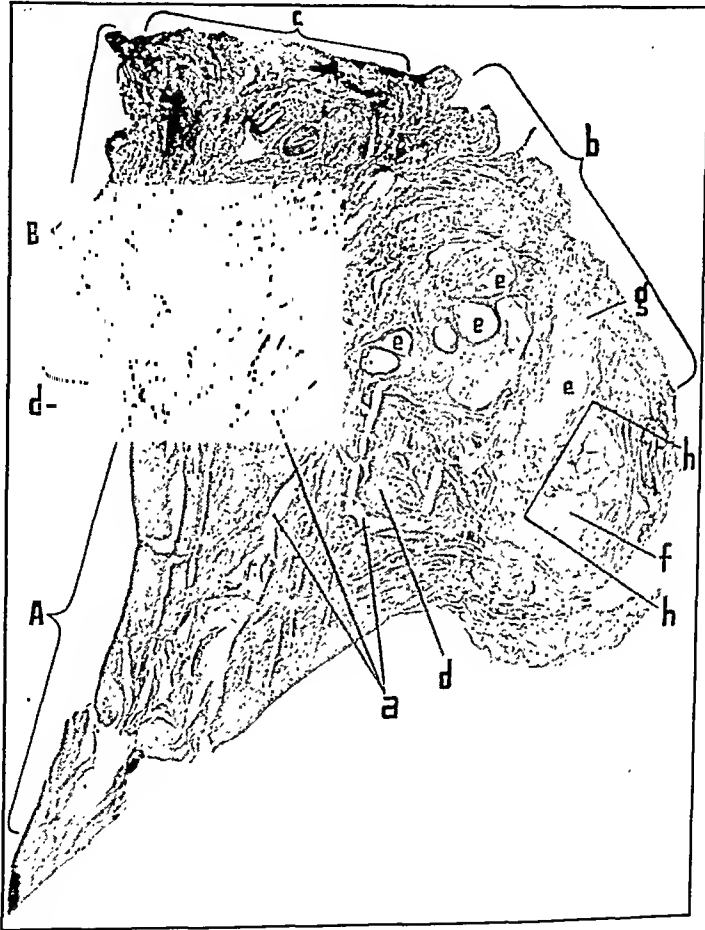


Fig. 2 (case 1).—Cross section of the cartilage and cyst, $\times 5$. *A*, avascular portion, containing cartilage with (*a*) areas of degeneration in it. *B*, vascular portion, including the periphery of the cartilage (*d*), the cystic mass (*b*) and the capsulosynovial tissue (*c*). The cysts (*e*) are of different size; some of them have distinct walls (*e'*) while others are enlarging and coalescing, having no limiting membrane or a poorly defined one (*g*).

containing the cartilage, in which are to be found small areas of degeneration (*a*), and the vascular portion (*B*), in which are included the cystic mass (*b*), the capsule and synovial lining (*c*) and the periphery

of the cartilage (*d*). The cysts in places have well defined walls of connective tissue lined with flat cells (*e*). In other sections one notes connective tissue cells in the process of degeneration (*f*). The cysts are filled with mucinous material. The origin of this is uncertain. It may be the result of secretion of the lining cells, or it may arise from the liquefaction of the connective tissue and lining cells, that is, it may

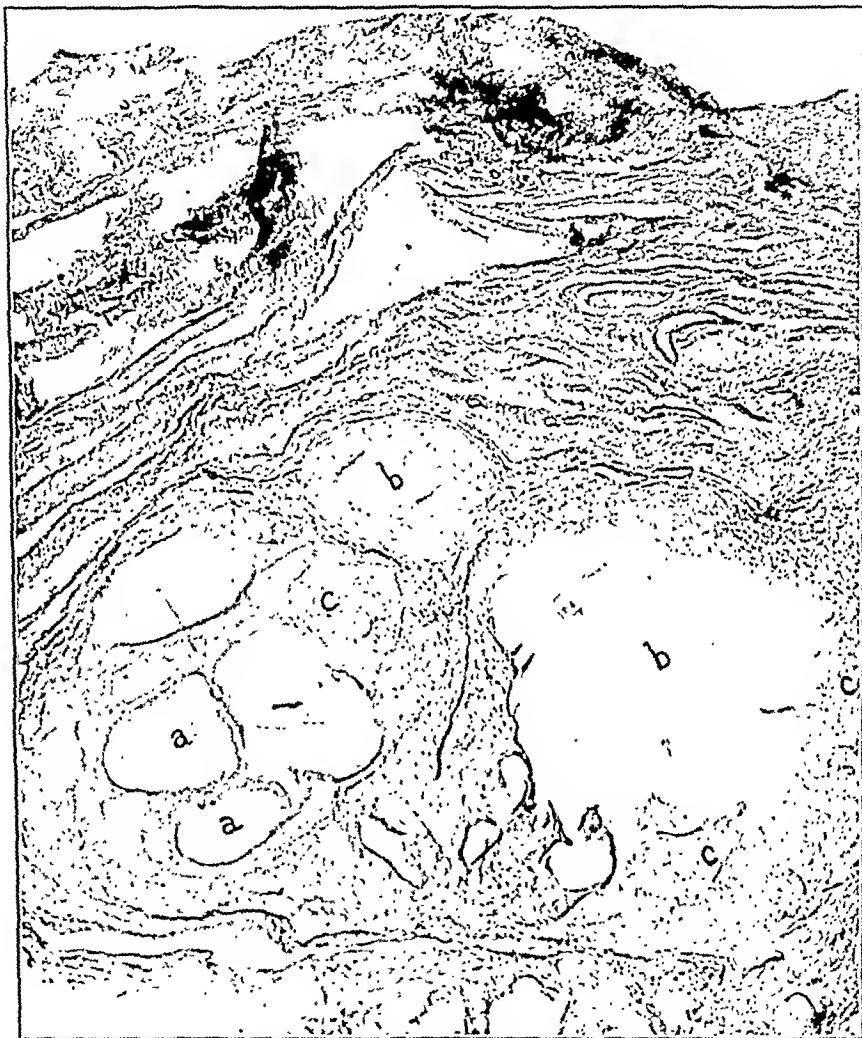


Fig. 3 (case 1).—Enlargement ($\times 30$) of the section marked *hh'* in figure 2: *a*, cysts with lining membrane; *b*, cysts without distinct lining cells, in the process of formation and enlargement; *c*, degenerating connective tissue cells.

be a product of degeneration. The cells of the lining membrane of the cysts are histologically analogous to those of the synovial tissue; this fact suggests the possibility of traumatic isolation and enclosure of some of the synovial tissue, which in its growth may form cysts and encroach on the cartilage.

REPORT OF CASES

CASE 1.—N. K., a man aged 27, was referred to me in September 1936. His chief complaint was of pain and swelling on the outer side of the right knee. The symptoms had first appeared about two years previously, following a fast game of handball. He began to have pains in the lateral aspect of the right knee joint. Several weeks later a swelling appeared in this region. The pain was increased by weight bearing and relieved by rest. At times the knee gave way suddenly, as a result of which the patient had cultivated the habit of rising from the sitting position with the knee completely extended, thus avoiding the likelihood of falling. He had never had any locking of the knee.

Examination showed a swelling on the outer side of the right knee, in the region of the external semilunar cartilage. The swelling was about 2 inches (5 cm.) in diameter and was moderately sensitive to pressure. On extension the mass almost completely disappeared, while on flexion it became conspicuous. Palpation revealed that the mass was intimately bound down to the deep tissues. A roentgen study of the knee gave negative results. A diagnosis of cyst of the external semilunar cartilage was made.

The patient was admitted to the Hospital for Joint Diseases, and operation was performed on October 12. A vertical incision 5 inches (12.5 cm.) in length was made over the outer aspect of the knee. The deep tissues were incised vertically, and a mass about the size of a pigeon's egg was seen at the joint line, in intimate association with the external semilunar cartilage. The cartilage and cyst were removed in one mass. The specimen showed that the cyst was part of the semilunar cartilage (figs. 1 and 2). The cut section of the gross specimen (fig. 1) showed a multilocular cystic mass. The report of the pathologist, Dr. Henry L. Jaffe, was as follows: "Gross examination: The specimen consists of an external semilunar cartilage considerably enlarged in its central portion, owing to cystic transformation of the parameniscal tissue [fig. 2]. Microscopic examination: The section shows a meniscus with parameniscal multilocular cysts. The meniscus itself shows considerable degeneration, with small cystic spaces [a in fig. 2 A] developing within its substance."

In this instance it may very well be that there was a primary degenerative process within the periphery of the cartilage, resulting from the degeneration of the cartilage cells. The cyst enlarged and advanced, causing further degeneration of the cartilage and involvement of the capsular tissue. The actual pathogenesis is nevertheless a matter of speculation.

This patient had an uneventful convalescence. The wound healed by primary union. At the time of writing the knee is stable and freely movable. The patient was reexamined on Dec. 15, 1937 and was found to be entirely cured.

CASE 2.—L. H. R., a man aged 34, was referred to me in June 1936. His chief complaint was of pain of about six months' duration on the outer side of the right knee. There was no known antecedent injury or illness. The pain, which appeared only when the patient was walking, was mild, and it disappeared in a week. It recurred periodically and with increasing severity. It was localized on the lateral side of the knee. There had been no "locking" and no effusion into the knee, but there was a clicking sensation when the knee was bent. Occasionally the knee "gave way" as if it had been kicked from under him, and he fell. There had been no limp, and the patient could walk as much as he pleased.

Examination showed an easily palpable, apparently fluctuating mass as large as a pigeon's egg on the outer side of the right knee, in the vicinity of the external semilunar cartilage. There was no local tenderness, and no evidence of inflammation was present. The mass was firmly attached to the deep tissues.

The skin and subcutaneous tissues were freely movable. A roentgen study of the knee revealed no pathologic change in the bone. A diagnosis of cyst of the external semilunar cartilage was made, and operation was performed on June 12. A short vertical incision was made over the anteroexternal aspect of the right knee, the middle of the incision being over the joint line. The incision was extended through the aponeurotic expansion of the vastus externus muscle. When the edges of this aponeurosis were retracted a mass about the size of a large marble was exposed. This was beneath and intimately bound down to the capsule of the joint. The joint capsule was incised transversely above and below the mass to permit removal of the cartilage and cyst *en masse*. The wound was closed in layers. An incision was made through the mass and the meniscus. The

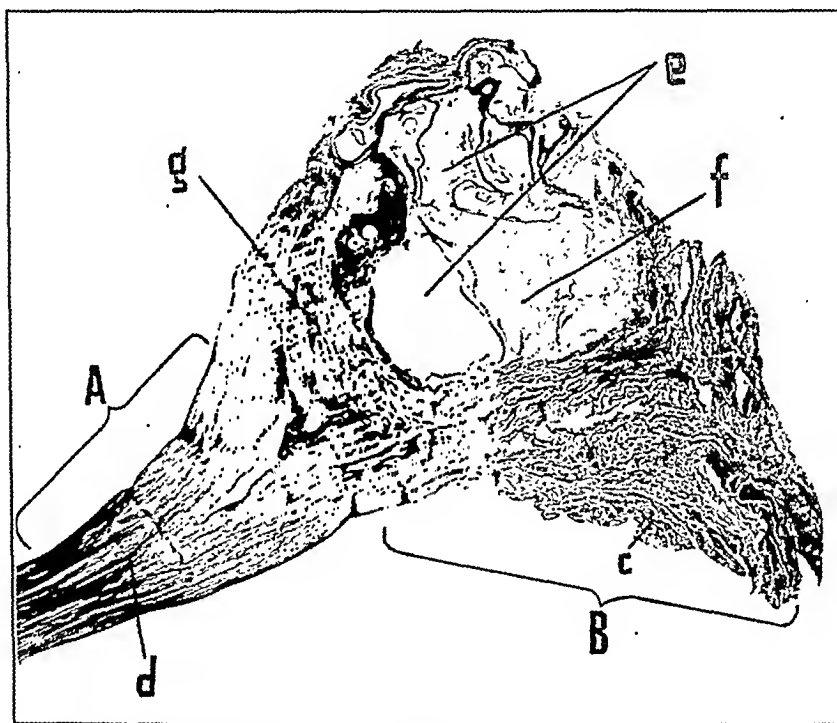


Fig. 4 (case 2).—Cross section ($\times 5$) through the largest diameter of the specimen: *A*, avascular portion of the meniscus; *B*, vascular portion containing the periphery of the meniscus, the cyst and the capsule; *c*, synovial membrane; *d*, areas of degeneration in the cartilage; *e*, cysts; *f*, mucinous material in the cyst; *g*, periphery of the cartilage.

mass was a multilocular cyst (fig. 4) containing glairy mucoid material. It was thoroughly embedded in the periphery of the fibrocartilage and was intimately attached to the capsule of the joint. Dr. Henry L. Jaffe reported on this specimen as follows: "Gross examination: The specimen consists of a somewhat enlarged meniscus. In the parameniscal tissue there is a multilocular, thin-walled cystic structure containing mucinous secretion. At one point, penetration of the cyst into the meniscus proper is observed. Microscopic examination: Sections show typical changes of parameniscal cyst formation with extension of the cyst to the meniscus proper. The meniscus itself shows degenerative changes, with tiny cystic spaces [fig. 4, *d*]. The extrameniscal cysts are in various stages of evolution. They apparently have arisen by liquefaction of degenerated and

softened connective tissue at the meniscocapsular border. These cysts are lined by flattened cells, apparently modified connective tissue cells. The tiny intrameniscal postdegenerative spaces are for the most part unlined."

This lesion was evidently the usual type of cyst of the external semilunar cartilage, beginning insidiously and progressing over a period of several months to a point at which it caused disability and sensitiveness of the knee joint. The histologic study gave no clue as to whether the cyst was first formed in the capsular tissue and then invaded the meniscus or whether it occurred immediately as a degenerative process of the meniscal tissue.

The operative result was entirely satisfactory. The wound healed *per primam intentionem*. The patient regained a normal range of motion and full control of the knee joint.

CASE 3.—C. B., a woman aged 19, was referred to me in January 1932 because of pain in the left knee. The pain had begun four years previously without any apparent cause. It appeared intermittently in more or less severe attacks. The attacks increased in severity, so that the patient finally sought medical aid. The pain was always increased by walking and relieved by rest. The patient stated that at times she was suddenly aware of "something slipping in the knee and getting out of place." When this occurred she flexed the knee acutely and was promptly relieved.

Examination showed that the patient walked without a limp. The left knee presented a distinct swelling on the outer aspect, in the region of the joint line, directly in front of the lateral ligament. The mass was cystic and fluctuant. It was somewhat tender to pressure. Flexion and extension of the knee were free. There was no abnormal anteroposterior, rotary or lateral motion. A diagnosis of cyst of the external semilunar cartilage was made. An operation was advised but was not performed by me. Attempts to trace this patient have been unsuccessful.

SUMMARY

Cyst of the external semilunar cartilages is a distinct entity which is easily diagnosed clinically. The lesion occurs chiefly in young adults, more frequently in males than in females. It is located in the meniscocapsular tissues. Its genesis is uncertain. As there is a history of injury in many cases, some surgeons believe that the lesion is initiated by an injury to the cartilage, as a result of which there is a hemorrhage with subsequent degeneration and liquefaction of the hematoma followed by cyst formation. Actually there are many cysts, some of which coalesce to form large cysts. Some are lined with a distinct connective tissue membrane covered with flat endothelial cells or perhaps with modified connective tissue cells resembling those which line synovial tissue. The lesion may represent a degenerative process in the meniscocapsular tissues, secondary to a vascular disturbance initiated by a trauma or other cause. Doubt as to whether trauma is an important etiologic factor arises from the fact that in the large number of cases of rupture and displacement of the semilunar cartilages caused by injury, no instance of a multilocular cyst has been observed. Fortunately the treatment is not dependent on knowledge of the cause. Removal of the cyst and the cartilage affords complete relief, and thus far no recurrence has been reported.

REVIEW OF UROLOGIC SURGERY

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(Concluded from Page 696)

PROSTATE GLAND

Physiology.—Farrell³⁵ described a method by which pure prostatic fluid may be obtained for study. The action of drugs on the prostate gland has been noted, as well as the response to electrical stimuli. The prostatic secretion of the dog is consistently acid. The secretion, as demonstrated by its intravenous injection or by perfusion experiments, has no great toxicity.

Many of the substances used therapeutically in urologic practice are secreted by the prostate gland. These substances do not appear to enhance the bactericidal action of the prostatic fluid. The normal prostatic fluid has a bactericidal action. The exact cause of this action is not known. Experiments are now being conducted to determine it.

Alcohol is eliminated by the prostate gland in measurable amounts. It has a deleterious action on the viability of sperm. Alcohol may be a factor in sterility.

35. Farrell, J. I.: The Newer Physiology of the Prostate Gland, *J. Urol.* 39:171-185 (Feb.) 1938.

Hypertrophy.—Mussnug³⁶ stated that damaged renal function in a patient with hypertrophy of the prostate gland is not always the result of residual urine and infection but that a toxic agent is also a factor. To prove this hypothesis he injected an extract of canine hypertrophic prostate gland into one series of dogs, and into another series he injected an extract of human hypertrophic prostate gland. There were two series for controls; one series was given injections of an extract of normal canine prostate gland, and the other was given extracts from other organs (the spleen, the liver, the thyroid gland, the musculature and the testis).

Regular examinations were made of the urine, the blood pressure and the concentration of urea in the blood, and the kidneys were examined microscopically at postmortem examination. The animals used as controls failed to show damaged renal function after the injections had been continued for half a year.

The animals given injections of extract of human and canine hypertrophic prostate gland all showed decreased renal function within a few weeks, which in many instances led to death. Anatomically Mussnug found a primary toxic injury of the glomeruli with secondary degenerative changes in the tubules. The changes were similar to the renal changes observed during pregnancy. In experiments performed with the animals under general anesthesia, when the ureter was exposed and an extract of hypertrophic prostate gland was injected intravenously, ureteral peristalsis was discontinued.

Mussnug concluded that the best procedure is to remove the hypertrophic prostate gland at operation as radically as possible in order to make sure of removal of the toxic focus.

Young³⁷ stated that transurethral operations have proved satisfactory in treatment of obstructive conditions at the vesical neck, particularly contractures, bars and moderate enlargements. When the disease has progressed much beyond this stage, according to statistics of a number of operators, enucleation of the prostate gland (preferably through the perineum) is the method of choice. By this means it is possible to see and feel the prostate gland, which is brought down by the tractor so that it may be examined carefully. A portion may even be excised for microscopic study if necessary. Thus the presence of early malignant changes may be detected and radical operation carried out. If the process is not malignant (in about 1 in 5 cases it is malignant) enucleation of the hypertrophied lobes from within the prostate gland may be carried out cleanly, the hemorrhage being completely

36. Mussnug, H.: Ueber die Entstehung der Nierenerkrankung bei Prostat hypertrophie, *Ztschr. f. urol. Chir. u. Gynäk.* **43**:497-526 (Jan.) 1938.

37. Young, H. H.: Some Problems in Surgical Treatment of the Prostate, *J. A. M. A.* **110**:280-283 (Jan. 22) 1938.

arrested by ligatures and sutures and the operative wound closed. This method provides a clean surgical technic, and one has the satisfaction of preventing sloughing and infection, which frequently persist for a considerable period after transurethral operations and lead to painful prostatitis in the remaining glandular tissue, to cystitis and to irritation; the symptoms of these conditions are frequently worse than those associated with obstruction.

Tillisch³⁸ reported a case of hyperplasia of the prostate gland. The patient, a man aged 29, came to the Mayo Clinic because of difficulty of urination. His present trouble had started several years before he was seen at the clinic and consisted of hesitancy in starting urination and scantiness of the urinary stream. There had been gradual increase in the severity of symptoms until one year previously, when severe frequency and urgency of urination had developed. A roentgenogram of the kidneys, ureters and bladder, taken elsewhere at that time, had revealed vesical calculi, which were removed cystoscopically. After this procedure the patient had complete relief of pain but frequency of urination continued, and he had nocturia (two to three times each night). There also was an increase in hesitancy; the stream became smaller, and the patient had the sensation of incomplete emptying of the bladder.

Examination of the prostate gland by rectum revealed a boggy gland, apparently normal in size. Results of urinalysis were negative. Cystoscopic examination revealed definite hypertrophy of the lateral lobe of the prostate gland, projecting anteriorly, and definite commissural enlargement. Transurethral resection was performed, and 4 Gm. of tissue was removed.

Thompson, in a discussion of the case, pointed out that an unusual feature is the fact that the obstructing tissue removed from the prostate gland, although the patient was only 29 years old, was similar to the adenofibromatous hyperplastic tissue which frequently causes obstruction of the prostatic urethra in elderly men. Tillisch's patient was the youngest patient with such a lesion to be seen at the clinic.

The cause of this patient's difficulty in urination was easily recognized through use of a cystoscope equipped with a system of retrograde lenses. The nodular appearance of the left lateral lobe of the prostate gland, which projected anteriorly, was grossly typical of adenomatous hyperplasia, and microscopic study of the removed tissue verified the impression.

Obstruction at the vesical neck rarely occurs in a young man. In the majority of cases either a median bar or a contracture of the vesical neck secondary to chronic prostatitis is present.

38. Tillisch, J. H.: Hyperplasia of the Prostate Gland: Report of an Unusual Case, *Proc. Staff Meet., Mayo Clin.* **13**:62-63 (Jan. 26) 1938.

Carcinoma.—Walthard³⁹ examined 100 prostate glands of men more than 40 years of age. The specimens were obtained at necropsy. None of the patients had died from disease of the prostate gland. The glands were cut in series, and every third section was examined. The results of this concise and thorough study are extremely interesting and influence one's views regarding prostatectomy.

In 30 cases Walthard observed an undeniable carcinoma of the prostate. In no case could the diagnosis be made before necropsy was performed, nor had the patient during his stay in the hospital shown any sign of prostatic malignant tumor. In 25 cases signs of malignant infiltration were observed; in 5 cases the typical picture of carcinoma was observed without any infiltrative growth into the regional tissue.

In the overwhelming majority of cases the carcinoma was in the prostate gland itself, that is, in the surgical capsule around the adenomatous nodules of the periurethral glands which form the surgical prostate gland. In 24 cases carcinoma occurred in its caudal part, between the colliculus seminalis and the caudal end of the gland, according to Young's findings. In 5 cases the carcinoma was situated both in the caudal third and in the middle third of the prostate gland, and in only 1 case was it near the bladder. In 4 instances carcinoma was observed in a benign nodule, but in 3 of these it could be demonstrated that the malignant growth had infiltrated the benign nodule only secondarily, from the outside.

As carcinoma and benign hypertrophy occur in patients of the same age groups, the surgeon can draw the following conclusions:

When an operation for hypertrophy of the prostate gland is necessary, there is a probability that carcinoma is concomitantly present in 30 per cent of cases. If it is desired to give prophylactic treatment for the carcinoma as well as to remove the obstacle to free outflow of urine, the perineal route should be used. From the point of view of prophylaxis, perineal prostatectomy is superior to transurethral resection or suprapubic enucleation. It is the only approach which gives a clear view of the prostate gland, allowing removal of the hypertrophied adenomatous nodules, as well as the anatomic prostate gland (the surgical capsule), extensively enough for sufficient prophylaxis. Although the mortality rate (4 per cent) of prostatic carcinoma can in no way be compared with the morbidity rate (30 per cent), one can never tell in which case the carcinoma may spread and cause clinical symptoms.

Chauvin⁴⁰ stated that no single form of treatment is applicable in all cases of cancer of the prostate. In cases in which the malignant

39. Walthard, B.: Die Häufigkeit und Histogenese des Prostatacarcinoms, *Ztschr. f. urol. Chir. u. Gynäk.* **43**:483-496 (Jan.) 1938.

40. Chauvin, E.: Cancer of the Prostate, *Kong. d. internat. Gesellsch. f. Urol* **2**:98-102, 1937.

tumor has developed but slightly, the growth is certainly amenable to surgical removal; this can be accomplished by simple enucleation (Freyer), often with simultaneous removal of the seminal vesicles, which may have been invaded.

A tumor of moderate development offers a more difficult problem. In the presence of such a tumor the capsule is invaded or even transcended but the tumor remains well limited. Wide prostatectomy, whether transvesical (Pauchet) or perineal (Young), is too grave an operation (46 per cent mortality); in addition, it destroys the sphincters, leaving the patient incontinent, and does not remove the danger of metastatic foci causing extension, especially in the bone. Chauvin has given up such destructive operations in favor of the use of radium, which is a valuable remedy and is attended with less risk. He disposes of the objections that it is horribly painful, that it is ineffective, that it encourages metastasis and that it is useless. It is not painful, or at most it causes very little pain, if applied by the perineal route. It is ineffective only when the technic is faulty. Irradiation must be homogeneous and prolonged; all parts of the tumor must receive an equal dose, and applications must be maintained for eight or ten days. The needles must carry a charge not exceeding 2 mg. of radium element.

Chauvin has treated 56 patients by this method, with only 3 failures and 3 recurrences. As for metastasis, it, too, is caused by faulty technic, inadequate doses and uneven application. If radium is properly applied, metastasis is not more extensive after its use than after surgical extirpation and is possibly less so. Radium therapy cannot be called useless when the alternative is retention of urine, followed by the slow agony that is the lot of a patient on whom cystostomy is performed.

Although cures by radium therapy are rare, they are nevertheless possible, in so far as one may speak of a cure of cancer. Chauvin recorded his results as follows: Among 56 patients treated with radium there were only 5 deaths (8.9 per cent). Application of radium caused little discomfort when it was not made intravesically; there was none of the intense vesical tenesmus reported by certain authors. The action of the radium was surprising in its rapidity, its definiteness and, one might almost say, its constancy. After removal of the needles the lesions were found to be destroyed: there were no more nodules and no inequalities of form or consistency. The tumor was replaced by a uniform mass, dense but not hard, which formed a lining behind the symphysis. In only 4 cases did failure occur. Late results were still more interesting. Recurrences in situ are exceptional in such cases; Chauvin has had only 4. Metastasis appears to be more frequent. Its incidence cannot be determined with any exactitude, because patients with this condition come only exceptionally into the urologic service. With

radium, as with the knife, one may expect only purely local action. Chauvin has seen 2 of his patients in perfect health five and six years, respectively, after treatment.

Functional results were good in the great majority of cases. Almost normal micturition resulted in cases of chronic retention and ischuria; cystostomy was necessary in only 6 cases. These results were obtained at the expense of discomfort which is insignificant when one considers the gravity of surgical intervention and the suffering caused by it.

For a tumor of the third stage, which has cleared the capsule and has advanced to any extent into the pelvis, nothing is to be expected from the use of radium. Only palliative therapy is applicable.

Pasteau,⁴¹ like others, made many attempts to find clinical signs that would lead to a definite early diagnosis of cancer of the prostate gland, but he failed. He stated that in his opinion the radical operation is not advisable. He stated also that treatment with roentgen rays or radium is not followed by cure but is, on the contrary, followed by intense pain and by accelerated extension of the malignant process. He has adopted the following course:

1. Because a prostate gland removed with a diagnosis of simple hypertrophy frequently contains nodules of malignant degeneration and because with such a condition suprapubic prostatectomy is followed by cure or by such long survival without pain or complications that one may speak clinically of cure, immediate and rapid prostatectomy is recommended when there is any doubt as to the nature of the lesion. The surgeon who makes it a practice to remove a prostate gland for simple hypertrophy is, in effect, controlling cancer of the prostate gland.

2. When the diagnosis of cancer is almost certain, it is better not to arouse illusory hope in the patient by surgical intervention. Radium and roentgen therapy, in view of their poor results are not recommended. The mechanical complications caused by retention should be cared for, and when retention occurs the bladder should be drained by suprapubic cystostomy. Precautions should be taken to assure subsequent cleanliness, this being the best means of preventing the severe infection which may occur when the bladder is not sufficiently emptied. Thus the fatal termination is retarded as much as possible, and the patient is saved from needless pain.

Lasio⁴² stated that treatment of cancer of the prostate gland, after the illusory results given by major operative methods, has in the last decade turned to physical therapy and especially to the use of roentgen rays and radium.

41. Pasteau, O.: Cancer of the Prostate, *Kong. d. internat. Gesellsch. f. Urol.* 2:96-98, 1937.

42. Lasio, G. B.: Treatment of Cancer of the Prostate, *Kong. d. internat. Gesellsch. f. Urol.* 2:124-130, 1937.

From an etiologic point of view, three main varieties of cancer of the prostate gland can be distinguished: (1) primary prostatic cancer in an organ which has not been invaded previously by any other kind of neoplasm, (2) cancer in an adenomatous prostate gland, and (3) cancer of the capsule of the prostate gland, or, more precisely, cancer developing in the fibroadenomatous glandular capsule of a prostatic adenoma that has been extirpated or that has not yet been operated on.

Lasio explained cancer as degeneration of the adenoma or as the result of irritation, degeneration and atypical proliferation of the epithelial cells of the true prostate gland. He reviewed all the symptoms in an effort to find signs that might aid in early diagnosis but concluded that this is still impossible. Such means as are available allow the discovery of the cancer only after it has reached a stage too advanced for any attempt at radical cure.

Lasio's personal observations were based on 1,855 cases of adenoma of the prostate gland, in 155 of which a beginning carcinoma was found. This material, however, did not lend itself well to the solution of problems concerning pathogenesis; it happened either that only the adenoma and not its capsule was examined microscopically, or the adenoma was found absolutely free from cancerous degeneration (the proper study of which would require the examination of serial sections throughout the entire organ, which has never been rigorously done, according to any statistics published).

It may be considered proved that from unquestionably benign hypertrophy a malignant transformation may develop, just as a cancer may start from a vesical papilloma. The secret of operative success lies in early diagnosis, while the process is limited to the prostate gland and its involucrums, with guarantee of absence of lymphatic metastasis. Clinical methods are not equal to this task. No method now exists which enables the surgeon to arrive at an early diagnosis. To this fact Lasio attributed the failures following his operations, results which, he stated, are shared by the majority of surgeons.

In cases of retention, permanent cystotomy is indicated to relieve suffering and to prevent infection; the exclusion of the cancerigenic zone arrests to some extent the development of the cancer, which is no longer subjected to irritative functional, instrumental and septic stimuli. Fifty per cent of Lasio's patients who were operated on received great benefit from this treatment, so that they gained in weight and in some cases asked for closure of the fistula, believing themselves cured.

The hypogastric route offers the advantage of permitting direct application of radium and roentgen rays, but Lasio's results were so poor that he gave up the method. Application of radium by way of the urethra gave a good local result but accomplished nothing definitive. The outcome in 2 cases in which radium was placed in the bed of the

adenectomized prostate gland was fatal within one and three months, respectively. Transvesical prostatectomy followed by radium therapy by way of the hypogastrium and the urethra was followed by death in two months; the same treatment with application of radium in the hypogastrium and the perineum prolonged life for six months. Perineotomy with infixation of needles by way of the perineal route in 3 cases was followed in 2 by death within a year and in 1 by clinical improvement but by no local effect.

Results of this kind are not encouraging, and Lasio concluded that new experiments must be tried if better results are to be obtained.

Bonanome⁴³ reviewed the statistics concerning 952 patients with disease of the prostate gland treated in his clinic at Rome, Italy. Eight hundred and fifty of these had prostatic hypertrophy, and 102 had cancer of the prostate gland. Of the cases in which cancer was present, the diagnosis was certain in 66; in the other 36, operative and histologic control was wanting. In terms of percentage of the whole, the cases of cancer constitute 12 per cent of the series, which decreases to 7.7 per cent if only the 66 fully proved cases are considered. These figures are not far from those of Ascoli (7.7 per cent) and of Blatt (7 per cent) but are far below those of Mingazzini (21 per cent) and of Young (18 per cent). All these figures might be increased if it were possible to compile, in addition, statistics regarding the later evolution of the cases, including the histologic reports. The difficulty of making a differential diagnosis between chronic prostatitis and cancer of the prostate gland is well known.

If it were possible to distinguish clinically between cancer derived from the submucous glands of the vesical neck and cancer derived from the true prostate gland, the first could be treated with enucleation, as in the case of ordinary prostatic hypertrophy, provided that operation was done early and metastasis had not occurred. In the treatment of cancer of the true prostate gland Bonanome has abstained from radical operation and has addressed himself to the relief of certain symptoms, such as retention, dysuria, ischuria and hematuria, by performing cystotomy or by use of transurethral electrotomy associated with roentgen therapy. Pollakiuria is greatly benefited by roentgen therapy; in some of the author's cases it disappeared in two days, with diminution or cessation of burning and pain on urination. The jet increased in force and caliber, and the general condition of the patient improved greatly. In some cases, however, benefit does not follow this treatment.

The behavior of metastatic foci in bone is interesting, such foci having been sensitive to irradiation. In 1 case, in which there was

43. Bonanome, A. L.: Treatment of Prostatic Cancer, *Kong. d. internat. Gesellsch. f. Urol.* 2:132-136, 1937.

bilateral sciatica and in which roentgen examination of the spinal column and the pelvis revealed typical dissemination of osteoplastic metastases, rectal examination established the existence of a small nodule that was undoubtedly carcinomatous. Roentgen therapy addressed to the metastatic foci caused gradual disappearance of the excruciating pain to such an extent that the patient was able to give up the use of morphine. He was still free from pain when examined five years later.

The method of irradiation is that of Coutard, with prolonged sittings and large doses. Usually 5,000 to 7,000 roentgens is given, the territory being divided into five fields: two suprapubic (with crossed foci) two sacral (with similarly crossed foci) and one perineal. In each field 1,000 to 1,300 roentgens is distributed, with 200 roentgens per application. Applications are given twice a day if a reaction does not occur. A cycle of treatment lasting about two weeks is given, if well tolerated; this is repeated every six months or may be repeated in three months if indicated.

Chevassu⁴⁴ expressed the opinion that in view of the slow evolution of cancer of the prostate gland in many cases it is difficult to assert that a service has been rendered to a patient when the treatment has done nothing more than permit him to live a few years longer. Lasting cures under histologic control are altogether exceptional.

For a good many years Chevassu has not used the dangerous radical operation but has used radium therapy. He has planted needles simultaneously at the back of the prostate gland (after prerectal décollement) and at the top by way of the bladder (after a cystostomy had been performed and the wound left open). By this method he had obtained complete clinical obliteration of the cancerous indurations. He has never seen, however, a single definite cure. The patient of whose condition he was most proud suddenly succumbed to paraplegia, and roentgen examination revealed an "ivory vertebra" that was beyond doubt neoplastic.

As the result of these experiences, at present he either employs no surgical treatment or does a prophylactic cystostomy. He admitted that the inadequacy of this treatment is lamentable but stated that he knows of no better way. He stated his definite opposition to the use of partial resections, saying that if the tumor is really cancer such a procedure is likely to act as a whip to speed its progress. He spoke of true cancer of the prostate gland and did not discuss prostatic hypertrophy associated with so-called nodules of neoplastic degeneration. It is always difficult to affirm that adenomatous zones in a state of proliferation in prostatic hypertrophy, examined after extirpation, are

44. Chevassu, M.: Treatment of Cancer of the Prostate, Kong. d. internat. Gesellsch. f. Urol. 2:114-120, 1937.

really cancer, and statistics on prostatic cancer cannot be based on observations of this kind. He expressed agreement with Oreja that all men more than 50 years of age should be examined systematically by rectum in order to assure early diagnosis.

For differential diagnosis between chronic prostatitis and cancer, retrograde urethroprostatography is today available, for in cases of prostatitis it is usual for one or more intraprostatic caverns to appear in the picture. Chevassu's experience with this method of exploration has shown him that among old men who have a hard, immovable prostate gland, cancer is the more frequent of these two conditions; chronic prostatitis, however, is not exceptional. Although this method readily permits recognition of chronic prostatitis, the images are so variable for cancer that it is often difficult to diagnose the latter with certainty. Everything depends on the relation of the cancer to the urethral canal. In cases of advanced cancer the urethra presents ulcerous and vegetating lesions with irregular outlines that do not resemble those of prostatic hypertrophy. In other cases, however, the urethra appears practically normal. Chevassu illustrated on the screen a case in which a normal urethra was projected on a skeleton of the pelvis, packed with neoplastic nodules caused by cancer (diagnosis proved at necropsy). He concluded that when a hard, nontuberculous prostate gland shows no caverns on urethrographic examination, cancer should be considered present if the induration does not yield to hot rectal lavages and to antisymphilitic treatment. He did not venture to say what form of treatment under such conditions is the wisest to carry out, even when diagnosed early.

Retrograde urethroprostatographic study with iodized poppyseed oil has never given rise to untoward symptoms in a series of 800 cases in which it has been used since 1933. Iodized poppyseed oil should never be used in a bleeding urethra, and retrograde urethroprostatographic examination should always be performed under fluoroscopic control. When employed with proper technic it is a remarkable method of examination.

Keyes⁴⁵ stated, in a discussion of papers by Hryntschak, Nitch and Oreja, that the clinical meaning of the term "early" will vary with each generation of urologists. Today one considers as an "early" cancer one which has not extended palpably beyond the prostate gland. Such a cancer may belong to any of three types.

1. Cancer arising within a hypertrophied portion of the gland; such a growth is removed entirely by prostatectomy for adenoma. Every surgeon knows by experience that sections of an ablated adenoma

45. Keyes, E. L., in discussion on Symposium on Treatment of Cancer of the Prostate, Kong. d. internat. Gesellsch. f. Urol. 2:92-94, 1937.

may reveal a small central carcinoma the existence of which had not been suspected. One expects that a patient after such ablation will not show further evidence of cancer.

2. Cancer which can be felt by rectum as an irregularity on the posterior surface of the gland. Such an irregularity, however, may be suggestive of chronic prostatitis rather than of carcinoma.

3. Cancer plainly palpable as such by rectal palpation against a sound in the urethra. In a large proportion of cases of such involvement metastasis has already occurred.

It will doubtless be necessary in the future to restrict the term "early" to the first two classes of cancer: (1) cancer discovered by the pathologist (postprostatectomy), and (2) cancer not to be distinguished as cancer by rectal palpation, even if this is made against a sound in the urethra.

Keyes stated that his first implantation of radon was performed in May 1931. His third patient, operated on in October 1931, was alive and seemingly well at the time of writing. There were no five year cures. Of his 14 patients operated on more than three years prior to his report, 4 were alive and well, and these 4 were the only ones among the 14 whose condition was diagnosed at biopsy while rectal palpation still gave a doubtful impression.

In the last three years, 27 patients with cancer have been operated on by various surgeons, with 1 postoperative death. The condition in 10 cases was diagnosed by aspiration biopsy while still not positively diagnosed by rectal palpation. Four of the patients died; 1 had a recurrence after twenty-six months; 5 were alive and well fourteen to twenty-four months after operation.

Of the 17 patients operated on in the last three years after the prostate gland was definitely cancerous to palpation, 6 were dead, 4 were alive but had recurrence (at sixteen, twenty-three, twenty-five and thirty months respectively); and 4 were alive and well fifteen to twenty-four months after operation.

Prostatitis.—Wesson⁴⁶ stated that infection of the prostate gland and seminal vesicles should be considered as one disease, because any condition involving the one almost invariably involves the other.

Acute prostatitis is generally caused by urethral instrumentation, by acute nonspecific urethritis or by cystitis. Chronic prostatitis is as frequent as chronic tonsillitis. It is a pyogenic infection originating in direct extension from the urethra or in invasion through the blood stream or the lymphatic vessels.

46. Wesson, M. B.: Symptoms of Non-Venereal Acute and Chronic Prostatitis, J. Urol. 39:135-144 (Feb.) 1938.

Symptoms of prostatitis and seminal vesiculitis have been aptly described as pus, pain and rheumatism. A patient who has a pain in the lower part of the back or a pain in the groin, extending suprapubically toward the midline, below the umbilicus or down into the scrotum, who has a prostate gland and seminal vesicles that are nodular and indurated on palpation, whose prostatic secretion contains pus and dead spermatozoa and who complains of exacerbation of the pain on massage does not have a beginning hernia or "sacroiliac slip." He has a prostatic backache.

Prostatitis usually does not cause sexual disturbances, but it may be responsible for every phase of derangement, from mild inaptitude to complete impotence.

Pain may be local or referred. It may be only a sense of discomfort, an ache, a dull sensation of soreness, a stiffness, a burning sensation, a tired feeling or a "bearing down," or dragging, sensation. Perineal, testicular and anal pain is present in some degree in practically all cases; usually there is thickening of the vas deferens and infiltration of the epididymis. Frequently there is a complaint of fulness, itching and burning about the anal orifice. Because of the close relation between the seminal vesicles, the ureters and the peritoneum, abdominal symptoms are frequent.

Intestinal obstruction alleged to be secondary to pressure of swollen seminal vesicles but probably caused by an adynamic ileus has been reported. Pressure on the ureters by the inflamed vas deferens or seminal vesicles customarily results in symptoms usually associated with the presence of stones and strictures.

Haven⁴⁷ stated that chronic pyogenic prostatitis can be a focus in producing ocular inflammations of nonspecific, endogenous origin. A focus of infection produces an endogenous lesion of the eye. It may be due to the transfer of bacteria or of bacterial toxins. Recent experimental work indicates the possibility of involvement of an allergic phenomenon. The tonsils are more frequently foci of infection than are the sinuses.

Nonspecific lesions of the eye respond well to nonspecific shock therapy by the injection of milk, diphtheria antitoxin or triple typhoid vaccine. Endogenous ocular inflammation of nonspecific origin may be aggravated by too vigorous prostatic massage. Increase in ocular inflammation after prostatic massage is diagnostic, indicating that the prostate gland is the focus of infection.

One sterile prostatic smear does not mean that chronic prostatic infection is not present. Chronic pyogenic prostatitis is oftener of

47. Haven, W. K.: The Relationship of Lesions of the Nose, Throat, Accessory Sinuses and the Eye to Chronic Pyogenic Prostatitis, *J. Urol.* **39**:128-134 (Feb.) 1938.

hematogenous than of urinary origin. Chronic pyogenic prostatitis responds more readily to local treatment after all foci are eliminated, including those in the tonsils and sinuses.

In discussing the causes of chronic prostatic infection, Cumming and Chittenden⁴⁸ stated that 98 per cent of their patients have one or more definite foci of infection.

In general, their treatment is based on cultural and serologic investigations and, except in determination of the use of palliative measures, the prostate gland is a secondary consideration. If tonsils or tags left after tonsillectomy harbor antigenic organisms, their removal is imperative, regardless of the age of the patient. The nasal sinuses if infected are treated. Devitalized teeth are extracted, and peridental infection requires accurate eradication.

The intestinal tract is often a major focus of infection.

Cumming and Chittenden concluded that much of the direct treatment administered to the prostate gland is unsound and unwise. Heat applied in any form to the rectum is comforting to the patient but otherwise is of questionable value. Routine prostatic massage, irrigations and endoscopic applications of silver nitrate fall into much the same category. Intraprostatic injections of mercurochrome, of hypertonic saline solution and of whole blood have been unsatisfactory in the experience of the authors, and the experimental work of O'Connor and Ladd has made them realize more fully the dangers of this method.

At first there was a tendency to consider the staphylococci as contaminants in the prostatic secretion, but now they have assumed a dominant position, and every effort is made to eliminate such organisms. If staphylococci are present, the patient is given a course of three to six intravenous injections of neoarsphenamine. Recently, the authors have begun to use antistaphylococcus serum in small doses (1 to 2.5 cc.) at intervals of five or six days until a total dose of about 5,000 units has been given. If colon bacilli are found in the urinary or prostatic cultures, mandelic acid is administered. If antigenic streptococci (either hemolytic or nonhemolytic) are present, the patient is given sulfanilamide.

Cumming and Chittenden considered five factors as their criteria of "cure": (1) complete relief of symptoms, (2) normal cytologic character of the prostatic fluid, (3) sterile cultures and smears of the prostatic fluid, (4) satisfactory removal of all infected foci, and (5) normal or relatively normal antibody patterns.

About 75 to 80 per cent of patients may be relieved, at least temporarily, by some form of treatment, especially by rectal heat therapy.

48. Cumming, R. E., and Chittenden, G. E.: Pyogenic Prostatitis: A Clinical Analysis of the Immune Response, *J. Urol.* **39**:118-122 (Feb.) 1938.

In the remainder, symptoms may persist despite every therapeutic measure. In the author's series the patients have been relieved of symptoms in 90 to 95 per cent of cases.

Reversion to a cytologically normal and culturally sterile prostatic fluid is often difficult to obtain and is usually impossible without complete and satisfactory removal of the toxic foci.

Prostatic Injection.—Lovelace and Emmett⁴⁹ reported their experience with the injection of sylnasol into the left lateral lobe of the prostate gland in 8 dogs. Sodium psylliate (sylnasol) is a solution frequently employed for treatment of inguinal hernia by injection. In each case, approximately 6 cc. of the solution was injected into the left lobe of the prostate gland and divided among three sites of injection. Injection was not made into the right lobe; this served as a control. Two dogs were examined eight hours after the injection, and the remainder were examined at periods varying from two to twelve months after the injection. Evidence of urinary obstruction was not found, and symptoms did not occur. The prostate glands removed eight hours after the injection revealed definite small areas of necrosis where the sodium psylliate was injected. In each of the remaining prostate glands removed there was striking reduction in the size of the lobe into which the solution had been injected. In each instance the left lobe was approximately one-half to one-third the size of the right lobe. Evidence of loss of tissue was not found, and the reduction in size seemed to be associated with an increase in the connective tissue stroma.

Changes After Operation.—Zide⁵⁰ examined microscopically the tissue removed in 85 cases of benign prostatic hypertrophy in which two or more transurethral or suprapubic operations had been performed at the Mayo Clinic at intervals of three months or more. This study was undertaken for the purpose of determining whether operations on the prostate gland have any histologic effect on the portion of the gland that remains. In 11 of the 85 cases the initial operation had been suprapubic prostatectomy, and in the remaining 74 cases transurethral resection had been performed. The shortest interval between the first and second operation was three months, and the longest, sixteen years. Practically all of the transurethral resections were performed with the Braasch-Bumpus instrument. The tissue obtained was studied from the point of view of infection, malignancy and changes in character and amount of parenchyma, smooth muscle and fibrous stroma.

49. Lovelace, W. R., and Emmett, J. L.: Intraprostatic Injection of Sclerosing Solutions: An Experimental Study, *Proc. Staff Meet., Mayo Clin.* **13**:196 (March 30) 1938.

50. Zide, H. A.: Changes in Prostatic Tissue After Operation, *Proc. Staff Meet., Mayo Clin.* **12**:269-272 (Dec. 8) 1937.

Zide arrived at the following conclusions: 1. Evidence of a carcinomatous tendency in the remaining prostatic tissue after transurethral resection greater than that following suprapubic enucleation is not apparent. In none of his series of cases were signs of malignant change found. 2. The incidence of prostatitis occurring after transurethral resection is not high. 3. In the majority of cases the prostatic tissue removed because of recurrent obstruction resembled closely that obtained at the primary operation, regardless of whether suprapubic enucleation or transurethral resection had been performed.

BLADDER

Tumor.—Cabot and Pace⁵¹ discussed the treatment of patients with extensive cancer of high malignancy in the bladder and patients with large malignant lesions of low grade for which transurethral treatment is inadequate. They emphasized the importance of accurate preoperative data as the most valuable aid in determination of the exact type of operative treatment best suited to each patient. Because of the wide variety of surgical procedures that may be carried out, it is important to determine as accurately as possible what procedure is indicated. This is often difficult, because preoperative data are not always entirely accurate. Estimation of the size and position of the tumor depends on the experience of the cystoscopist to a large extent, and it is always difficult to determine cystoscopically the extent of involvement of the deeper layers of the bladder and the ureters. Likewise, it is difficult to determine preoperatively whether or not the lesion has extended through the wall of the bladder and has involved the adjacent structures. There are three main preoperative diagnostic measures which should be utilized in every case, namely: (1) cystoscopic examination, (2) cystographic examination and (3) intravenous urographic examination.

Cabot and Pace based their observations on 46 cases in which suprapubic operation for vesical neoplasm had recently been performed at the Mayo Clinic. Cystoscopic examination is of importance in determination of the presence of the tumor and also (by removal of appropriate specimens) of the type, grade, position and extent of the lesion. It is particularly useful in determination of the situation of the mass in relation to the ureters and to the vesical neck. Diagnosis from cystoscopic biopsy is not invariably accurate; however, with rare exceptions, the grade and type of lesion as determined by biopsy are observed in subsequent pathologic examinations to be remarkably accurate. In the group of 46 cases reviewed, opinions formed at the time of cysto-

51. Cabot, H., and Pace, J. M.: Methods of Selecting the Proper Operative Treatment for Cancer of the Bladder, *Tr. Am. A. Genito-Urin. Surgeons* 30: 235-248, 1937.

scopic study were almost precisely correct in 26, more or less incorrect in 19 and vague in 1, when judged by the findings at suprapubic exploration.

The cystogram is most helpful in estimation of the extent of vesical involvement as shown by filling defects. In a certain number of cases a cystogram is suggestive of considerably more extensive involvement than would be noted from cystoscopic examination. Again, it may be helpful in the presence of a massive, pedunculated tumor of low grade, when an accurate cystoscopic estimate cannot be made of actual involvement of the vesical wall. Unfortunately, examination of the cystogram does not indicate in which cases the lesion has extended into the perivesical tissues and in which it is still confined to the vesical wall.

An intravenous urogram is of most value in demonstrating the presence or absence of obstruction to one or both ureters and the resultant effects of such obstruction on renal function. Obstruction of the ureters cannot be accurately determined in every case by cystoscopic examination, and an intravenous urogram is of inestimable value for this purpose. The use of intravenous urographic study also eliminates the necessity of catheterizing the ureters, which is not always possible or desirable.

Summarizing their opinions, Cabot and Pace concluded that cystoscopic study with the obtaining of appropriate material for pathologic study and the taking of an intravenous urogram are essential diagnostic measures in cases of vesical neoplasm. The retrograde cystogram is given second place in diagnosis, although its use is generally desirable. A classification of treatment follows.

1. *Suprapubic treatment.* Transvesical electrocoagulation is best suited to a bushy, papillomatous tumor of low grade, classified according to Broders' method as of grade 1 but often regarded as benign. It may also be applicable to a small sessile tumor classified as of grade 1 or 2, in which case it should generally be combined with implantation of radon.

Electrocoagulation is a purely palliative method of treatment for inoperable tumor and is used to control hemorrhage. The use of this method has been fairly widespread in the past. The authors expressed doubt as to whether it will remain a recognized treatment.

2. *Implantation of radon.* This measure, with or without preliminary or postoperative irradiation, has a definite place in the treatment of vesical tumor, but it is difficult to select cases in which its use is suitable. It is suitable for application to a tumor of high grade. It is important to determine whether the tumor to be treated with implantation of radon encroaches on the ureter, because such treatment should rarely, if ever, be applied if the ureter is grossly obstructed or if an extensive lesion exists.

3. Excision or segmental resection. "Excision" means removal of a circumscribed portion of the vesical wall. "Segmental resection" is defined as removal of a larger or smaller segment of the vesical wall, a suprapubic opening being used and resection being extended downward and laterally as far as necessary. Excision gives good results in cases in which there is little or no involvement of the deeper layers of the vesical wall and in which the lesion is relatively small. Segmental resection gives the best results in the treatment of a tumor of the vesical dome or of the lateral vesical wall.

4. Transplantation of the ureters to the bowel or to the skin. This type of operation is done either as a procedure preliminary to total cystectomy or as a palliative measure in cases of obstruction of both ureters. In the latter instance it may be followed by irradiation. Cabot and Pace concluded that ureteroenterostomy should be confined to cases in which gross abnormality of the ureters does not exist. Total cystectomy should be done in two stages, the ureters being transplanted to the intestine at the initial operation and the bladder being removed at the second. Cutaneous ureterostomy is largely reserved for patients with dilated ureters. The authors concluded that this operation has a wider scope of usefulness than has been realized in the United States. The records of 9 illustrative cases of vesical neoplasm were abstracted by the authors.

Randall and Uhle⁵² stated that the treatment of vesical carcinoma should be selective. Transvesical diathermy is of value in treatment of a lesion involving only the basal regions of the bladder or a lesion not amenable to vesical resection or to transurethral management.

The safety of transvesical diathermy is shown by an operative mortality rate of 9.8 per cent.

The three most important complications of the use of diathermy are: (1) establishment of a fistulous communication between the bladder and the rectum or vagina, (2) acute pyelonephritis, and (3) chronic pyelonephritis. A fistula can be prevented by curbing the overzealous application of current of high frequency. There was only 1 fistula (vesicovaginal) in Randall and Uhle's series. The incidence of acute pyelonephritis can be reduced by introduction of a ureteral catheter for drainage at the conclusion of the operation if diathermy has been applied directly over the ureteral orifice or in close proximity to it. Stenosis of the ureteral orifice, secondary to healing and fibrosis, is a later manifestation of the effects produced by surgical diathermy. Renal morbidity (chronic pyelonephritis) can be lessened by periodic ureteral dilation during the patient's convalescence.

52. Randall, A., and Uhle, C. A. W.: Transvesical Diathermy in the Treatment of Carcinoma of the Bladder, *Surg., Gynec. & Obst.* 66:927-932 (May) 1938.

Diathermy produces aseptic necrosis. If infection supervenes, the progression of pathologic events may range from the simple to the fulminating type, with pelvic cellulitis, pelvic phlebitis and death.

Cicatricial reaction following diathermy does not produce great vesical deformity. In spite of extensive diathermy, scarring is often minimal, and in 47 per cent of cases vesical comfort can be acquired.

There was a general mortality rate of 56.8 per cent. Death was ascribed to recurrence of the growth, with secondary renal infection and uremia. No evidence of recurrence, irrespective of the length of follow-up, was found in 35.3 per cent of cases. Recurrent growths developed in 43.1 per cent.

Routine cystoscopic study after operation is of great importance in detection of early or late recurrence. In 1 instance a papillary recurrence was found seventy-four months after the original operation. Cystoscopic fulguration is sufficient to effect control.

The importance of an efficient follow-up service cannot be overemphasized. Ten patients (19.6 per cent) were followed for forty to eighty-six months. Four had recurrences, and 6 were free of recurrence.

Randall and Uhle have been unable to substantiate the figures of Counseller and Braasch (88 per cent of patients living more than five years), but they felt that the results of diathermy in the treatment of carcinoma of the bladder are significant and should foster a wider clinical interest in this method of treatment.

Exstrophy.—Gaudin and Cabot⁵³ reported the case of a boy aged 1 month who had a small pedunculated tumor covered with mucosa. The tumor was situated in the midline, just above the symphysis pubis. It was spherical, red and glistening and was surrounded by skin which showed some evidence of irritation. There was no obvious drainage from the mass, which was soft and seemed slightly movable on the subjacent abdominal wall. The child urinated normally. Except for the tumor, no congenital abnormality was noted. The growth was removed by simple excision. There was no evidence of continuation of the mass into the interior, and it extended downward only to the subcutaneous tissue. The postoperative course was uneventful. Microscopic examination of the tissue removed showed it to be a portion of the bladder. Gaudin and Cabot discussed the embryologic considerations that enter into partial exstrophy of the bladder. They concluded that the difference between the anatomic conditions in the case presented and total extraversion of the bladder, with epispadias, is a matter only of degree of abnormality.

53. Gaudin, H. J., and Cabot, H.: Partial Exstrophy of the Bladder: Embryologic Considerations; Report of a Case, Proc. Staff Meet., Mayo Clin. 13:216-220 (April 6) 1938.

Cystitis Emphysematosa.—Wells⁵⁴ reported the results of 1,800 necropsies. He observed 7 typical cases of cystitis emphysematosa. He stated that he has no evidence that either glycosuria or vesical trauma is an essential factor in the production of this condition, although one or the other factor is present in many cases. In 5 of the 7 cases reported the patients were males. Wells' observations indicated that postmortem formation of gas is probably not responsible for this condition but gave no suggestion as to when or how it is usually produced. If cystitis emphysematosa is really much more frequent now than formerly, it may be owing to the greater frequency of vesical trauma from cystoscopy and catheterization or from the greater frequency of glycosuria in terminal states from therapeutic injections of dextrose. It probably has no important influence on the course of the patient's condition.

Decompression.—The idea that sudden emptying of the chronically distended bladder is dangerous is firmly established in the literature. Creevy⁵⁵ stated that the theories explaining such a danger fail to withstand critical analysis because at necropsy, in the absence of residual urine, lesions ascribable to sudden emptying of the chronically distended bladder cannot be distinguished from those due to infection. Eighty per cent of patients who die after catheterization succumb to pyelonephritis, either acute or chronic; 20 per cent succumb to infections outside the urinary tract. Sudden death after catheterization may be due to coincidental coronary thrombosis or to pulmonary embolism. The phenomena usually ascribed to sudden emptying of the bladder can be produced by pyelonephritis. Gradual decompression of the distended bladder did not reduce the mortality in a series of 120 cases as compared with that in a similar series in which sudden emptying was practiced. Gradual decompression should be abandoned. Its abandonment has not produced any untoward reactions in Creevy's experience.

Incontinence.—Meschede⁵⁶ recommended two operative procedures for the cure of traumatic incontinence in women; both gave him satisfactory results. For elderly women he used an operation involving interposition of the uterus; for younger women or hysterectomized women he used a plastic procedure with both bulbocavernous muscles and strips of fascia from the pyramidalis muscle. In this procedure muscles and fascia form a tight ring around the urethra. Meschede has been satisfied with his results to such an extent that he now uses these two methods in all cases.

54. Wells, H. G.: Report of Seven Cases of Cystitis Emphysematosa, *J. Urol.* **39**:391-397 (April) 1938.

55. Creevy, C. D.: Is Sudden Emptying of the Chronically Distended Bladder Dangerous? *J. Urol.* **39**:403-409 (April) 1938.

56. Meschede, H.: Zur Behebung der traumatischen Inkontinenz der Frauen. *Ztschr. f. urol. Chir. u. Gynäk.* **44**:22-25 (March 3) 1938.

Presacral Neurectomy.—Pearl and Strauss⁵⁷ stated that presacral neurectomy may establish voluntary micturition in cases of neurogenic vesical dysfunction with retention, in which there are weakness of the detrusor muscle and spasticity of the internal sphincter. However, the detrusor muscle may remain hypotonic, and the bladder may not empty completely.

Presacral neurectomy increases the expulsive force of the detrusor muscle and relaxes a spastic internal sphincter. This effect may be temporary.

Bilateral sacral ganglionectomy is advisable in addition to presacral neurectomy in the treatment of painful vesical conditions or when prolonged vasodilatation is desired in cases of severe, intractable cystitis. Undesirable effects have not been noted following presacral neurectomy and sacral ganglionectomy. At present, operations on the sympathetic nerves supplying the bladder should be considered experimental.

TESTICLE

Tumor.—Hinman and Powell,⁵⁸ in discussing the management of tumor of the testicle, pointed out that examination of the scrotal mass suspected of being a tumor should be carried out with a minimum of handling and squeezing. The test for gonadotropic substance aids materially in diagnosis. A negative result from the test, however, does not exclude the possibility that the tumor is malignant, because in about 20 per cent of the authors' cases urinary excretion of the gonadotropic substance did not occur. The danger of squeezing cells of a malignant tumor into the lymphatics is far greater at the time of examination than at orchidectomy when the operation is properly carried out through a high inguinal incision. The cord may be clamped and divided, all the lymphatic and vascular channels leading from the neoplasm being severed, before the neoplasm is handled. When the mass is removed, it should be examined for gonadotropic substance; information gained from such an examination, together with that from histologic examination and the previous urinary gonadotropic titer, makes it possible to classify the neoplasm, determine the prognosis and outline the extent of further treatment. It is also of aid in deciding whether such treatment is to be surgical, roentgenologic or both.

Hinman and Powell classified a group of neoplasms of the testicle from a glandular-histologic point of view into certain main types: embryonal mixed cell tumor (teratoma), embryonal carcinoma (uni-

57. Pearl, F. L., and Strauss, B.: Presacral Neurectomy and Sacral Ganglionectomy in Affections of the Bladder, *J. Urol.* **39**:645-661 (May) 1938.

58. Hinman, F., and Powell, T. O.: The Management of Tumor of the Testicle. *J. A. M. A.* **110**:188-190 (Jan. 15) 1938.

cellular) and the rare, nonembryonal and miscellaneous tumors. In an analysis of 58 cases in which tests for gonadotropic principle were made, there were 14 cases of embryonal teratoma. Only 1 patient lived five years. The response to irradiation in these cases was fair, but the prognosis as determined from the result obtained was extremely poor. There were 33 cases of embryonal carcinoma. In 7 of these the growths were regarded as primitive tumors causing high urinary gonadotropic excretion. In this group the response to irradiation was good, but only 2 patients lived two years after irradiation. The remaining embryonal carcinomas (histologically "seminomas") were regarded as examples of differentiated embryonal carcinoma and caused excretion of small amounts of gonadotropic substance. In this group of 26 cases the response to irradiation was good, and 22 of the patients were alive and apparently well at the time of the report, three to four years after irradiation. The prognosis in this group is regarded as good. There were 3 cases of benign adult teratoma. There were 8 cases of the same histologic description as the differentiated type of carcinoma, but in these there was no urinary gonadotropic excretion, and when the tumors were extracted it was shown that they were entirely void of the gonadotropic principle. These were considered as non-embryonal or adult tumors and were classified as "adult seminoma." There were 8 such tumors; only 1 patient was dead at the end of three years.

Two cases of tumor associated with unusually high urinary gonadotropic titer were reported. In both cases the gonadotropic titer of the urine reached 1,000,000 units per liter. The tumor in each case was regarded as primitive embryonal teratoma (chorioepithelioma). In both cases heavily filtered irradiation at 850 kilovolts was given. The patients lived about one year after the apparent onset of the disease.

Ferguson⁵⁹ disagreed with Hinman and Powell on the point of orchidectomy before irradiation. He conceded that the scientific information to be obtained by microscopic examination of the unaltered tumor and by assay of fresh tissue for gonadotropic substance is an advantage. However, this advantage carries little weight when it is seen that the clinical results obtained at the end of five years are better when irradiation precedes orchidectomy. In a review of the Memorial Hospital series of 292 teratomas of the testis, encountered between 1917 and 1929, it was found that of 14 patients who had primary operable tumors and were treated by irradiation before orchidectomy, 11 (78.5 per cent) were alive and without evidence of disease at the end of five years, whereas of 28 patients who had primary operable tumors and

59. Ferguson, R. S., in discussion on papers by Kreutzmann and Colloff, Hinman and Powell and Fetter, J. A. M. A. **110**:196-197 (Jan. 15) 1938.

on whom orchidectomy was performed before irradiation was given, only 12 (42.8 per cent) were alive and well without evidence of disease at the end of five years.

Ferguson admitted that with immediate irradiation after orchidectomy there may not be any difference in the results at the end of five years as compared with the results of irradiation before orchidectomy, but he stated that at present he feels that the advantage lies with pre-operative irradiation.

EPIDIDYMIS

Tumor.—Lazarus⁶⁰ stated that primary malignant tumor of the epididymis is rare, there being but 40 cases on record. Although such tumors have been classified under a variety of names, it seems that the majority of them, if subjected to an extremely critical analysis, would fall in the group of malignant teratoma in which one type of cell predominates to the exclusion of all other teratomatous elements. Summarizing the cases according to the authors' designations of the tumors, one finds 20 carcinomas and 17 sarcomas. Seventy-eight per cent of patients who stated the duration of their illness had had symptoms for longer than a month before they sought medical aid. Although 16 patients in this series did not mention pain, 75 per cent of the remaining patients had a definite history of pain either preceding or accompanying swelling in the testis. Only 15 of the 40 patients gave information concerning trauma, and 10 of these 15 patients stated that trauma had definitely antedated the appearance of the tumor.

Simple orchidectomy appears to have been the procedure of choice in the vast majority of collected cases. Lately, irradiation has been advocated as a valuable adjuvant to surgical management.

Regarding results, the survey lacked information concerning this feature in 10 cases. In the remaining 30 cases, 40 per cent of the patients were reported dead within two years of operation, and 27 per cent died within the first year.

INFECTIONS OF THE VAS DEFERENS

Kreutzmann⁶¹ stated that viable organisms may be present in the vas deferens without causing symptoms or producing gross changes. Epididymitis following ligation of the vas deferens is due to lighting up of a previous vasal infection and not to infection of the lymphatic vessels or the blood stream. Vasitis and epididymitis occur only in the presence of infected urine. Under certain conditions, reflux of urine

60. Lazarus, J. A.: Primary Malignant Tumor of the Epididymis, *J. Urol.* 39:751-765 (June) 1938.

61. Kreutzmann, H. A. R.: Studies of Infections of the Vas Deferens, *J. Urol.* 39:123-127 (Feb.) 1938.

may occur into the vas deferens as it does into the ureter. When the urine is infected, instrumentation doubles the probability of epididymitis. Chronic prostatitis alone will not cause vasitis or epididymitis.

EPISPADIAS

Cabot⁶² emphasized the fact that the number of different operations suggested for the correction of epispadias and hypospadias attests the lack of complete success with any one procedure. He described the technic for correction of epispadias either associated or unassociated with exstrophy. Correction of this abnormality has been difficult because of the partially separated corpora cavernosa. This condition often involves considerable tension when the urethra is formed from lateral flaps taken from the sides of the corpora, and failure may result.

Cabot discussed the disadvantages of certain procedures for correction of epispadias and then described a technic with his own modification. The urethra is constructed from the mucous membrane covering the dorsal surface of the penis. In order to provide a covering of skin for this newly formed canal, two transverse incisions are made in the scrotum, one at the penoscrotal juncture and one farther posteriorly. A tunnel of scrotal skin is thereby created, and the penis is inserted beneath it so that the flap of scrotal skin lies over the dorsal surface of the penis, where the new urethra has been formed. The penis should be left in this position for at least two or three weeks, at the end of which time the scrotal flap may be divided and the wound united in the midline of the scrotum by suture. Cabot's article is well illustrated by drawings.

SPERMATOCELE

Huggins and Noonan⁶³ stated that spermatocele arises as a result of partial obstruction of the sperm-conducting system and that vasotomy does not cause increase of its size. Spermatocele always contains spermatozoa and does not appear before puberty. The membrane is impermeable to phosphate in the direction from the plasma to the cyst and is permeable with difficulty in the opposite direction.

In the authors' cases, spermatocele always disappeared after application of roentgen therapy, without a significant decrease in the size of the testis and without loss of sexual potency or libido. With the doses used, 4 patients had spermatocele sixty days after treatment, and a second course of treatment was given, but this always was sufficient to

62. Cabot, H.: Treatment of Epispadias in the Male, *Proc. Staff Meet., Mayo Clin.* **12**:793-795 (Dec. 15) 1937.

63. Huggins, C., and Noonan, W. J.: Spermatocele, Including Its X-Ray Treatment, *J. Urol.* **39**:784-790 (June) 1938.

make the lesion recede permanently. Because sterilization occurs, roentgen therapy is advised only in case sterility is not undesirable, as when the patient is old.

UROGENITAL INFECTIONS

Anaerobic infection complicating surgical procedures on the urinary tract is infrequent. Yet the development of this type of infection is of such serious moment as to warrant emphasis of the importance of its early recognition and treatment. Mencher and Leiter⁶⁴ gave abstracts of 14 cases of postoperative anaerobic infection of the urinary tract, observed at the Mount Sinai Hospital, New York, during the past eleven years. Infection in 11 cases was due to *Bacillus welchii*, and in 3 cases typical symptoms of tetanus occurred.

The occurrence of postoperative anaerobic infection has always given rise to theoretic discussions as to the portals of entry. The following sources of contamination are to be considered: (1) the skin, (2) the rectum, (3) operative materials, and (4) urine, pus and urinary calculi.

The prognosis in cases of infection by *B. welchii* is directly dependent on early recognition and adequate treatment. If there is an inordinate rise in temperature, with or without symptoms of toxemia, careful inspection of the wound in addition to a general physical examination should be done. Discoloration, edema or crepitation in the region of the wound calls for further investigation of its depths. Crackling may be heard if firm pressure with the stethoscope is applied against the involved region in which gas is present.

Mencher and Leiter stated that under these circumstances they remove superficial and deep sutures, watching for serum, pus and air bubbles. Smears and cultures are immediately made, and if these yield bacteria, active therapy to combat the infection is instituted. The wound is split wide open, tubes and catheters are placed in the depths for continuous irrigation with hydrogen peroxide and oxygen, and large quantities of polyvalent *Bacillus perfringens* serum are administered intramuscularly, locally and even intravenously.

When the infection subsides, the use of diluted solution of sodium hypochlorite U.S.P. may be alternated with that of irrigations with hydrogen peroxide to hasten the separation of necrotic tissue and to stimulate the process of granulation.

Early recognition of tetanus is more difficult. General symptoms signify late manifestations of the disease. The appearance of the wound is not of aid in making the diagnosis. The mortality in cases of tetanus

64. Mencher, W. H., and Leiter, H. E.: *Anaerobic Infections Following Operations on the Urinary Tract*, Surg., Gynec. & Obst. 66:677-683 (March) 1938.

is appalling. Any hope of combating the complication depends on early diagnosis and administration of large doses of tetanus antitoxin by all routes.

Helmholz⁶⁵ stated that coccic infection occurs with equal frequency in the male and in the female. Bacillary infection of the female occurs three to four times as frequently as bacillary infection of the male. Coccal infection occurs by way of the blood stream, whereas bacillary infection occurs by other routes. The impossibility of infecting the normal bladder of man by introduction of bacteria through the urethra has its counterpart in inability to produce experimental infection of the bladder of the rabbit by injection of massive doses of bacteria. The greater frequency of bacillary infection in the female would lead to the belief that the infection occurs by way of the urethra, and although lymphogenous infection must be considered a possibility, there is no definite proof of its occurrence. At present it is impossible from study of material relevant to human beings to give any definite answer to the question. However, it is evident that two factors are necessary to cause infection of the bladder, namely, lowered resistance of the mucosa and bacterial invasion.

Experimental production of infection of the renal pelvis from the bladder has been accomplished by intracystic injection of bacteria into the bladder. The histologic picture of pelvic inflammation differs from that seen when the pelvis is infected by way of the blood stream. Histologic studies of the ureter have shown that in only 3 of 13 cases was there any evidence of periureteral inflammation. Therefore, unless it is assumed that infection can be spread by way of the periureteral lymphatic structures without leaving a trace behind, it must be assumed that in the other 10 cases the infection was spread by way of the lumen of the ureter. The same conclusion must be drawn concerning spontaneous pyelitis in rabbits, in which evidence of periureteral infiltration was found in only 6 of 16 cases. Taking this in conjunction with the work of David, which showed that periureteral inflammation does not necessarily mean that infection of the renal pelvis is present, Helmholz has assumed until more definite information is available that the usual spread of infection from the bladder to the pelvis is by way of the lumen of the ureter.

With stasis, the parenchyma of the kidney rapidly becomes infected from the pelvis by way of the perivascular lymphatic structures and by direct passage of the organisms through the pelvic lining over the parenchyma. Thrombosis forms an important feature of the renal

65. Helmholz, H. F.: Ascending Infection of the Urinary Passages, *Am. J. Surg.* **38**:18-28 (Oct.) 1937.

changes. Without stasis, infection of the pelvis tends to remain local, and only exceptionally does infection spread to the parenchyma by the same channels.

The striking difference between the two series of experiments would indicate that stasis is the all-important factor in producing ascent of infection from the renal pelvis to the renal parenchyma.

Nelson⁶⁶ stated that experimental and clinical findings justify the conclusion that cervical infection can and often does extend to the urinary tract. When the trisymptom complex to which reference has been made is present, the clinician should suspect cervicitis to be the primary cause of such symptoms. Infection in the deep portion of the cervix is sometimes not discernible to inspection or palpation. Cauterization usually fails to arrest extension of the infection from the cervix to the urinary tract. When properly performed for cervicitis that is causing urinary symptoms, the Sturmdorf type of operation usually brings about permanent relief.

Vest, Harrill and Colston⁶⁷ stated that administration of sulfanilamide is the most important forward step yet taken by scientific medicine in the treatment of gonorrhea and other urinary infections.

Sulfanilamide itself may be only the first of many efficacious and satisfactory new compounds, but with the vast problems yet to be elucidated concerning this drug, years will undoubtedly be required to produce results such as Ehrlich predicted. From research in all fields, chemical, biologic and clinical, there will undoubtedly evolve the ideal remedy as postulated by Ehrlich in 1913: "A remedy entirely innocuous in itself, which is not fixed by the organs of the body but which would, however, strike the parasites with full intensity."

Schulte⁶⁸ reviewed the literature on the development of sulfanilamide, which, he stated, is the product of numerous investigations extending over a period of thirty years. Domagk is given credit for the discovery of "prontosil," and Gelmo was the first to mention the drug now called sulfanilamide. Many other physicians contributed largely to the chemical developments which permitted the synthesis of these drugs. At present, a number of investigators are engaged in the further study of various compounds that might be used for chemotherapy.

66. Nelson, O. A.: Urinary Tract Disturbances Referable to Cervicitis, *J. Urol.* **39**:361-365 (March) 1938.

67. Vest, S. A.; Harrill, H., and Colston, J. A. C.: The Use of Sulfanilamide in Urogenital Infections, *J. Urol.* **39**:198-221 (Feb.) 1938.

68. Schulte, T. L.: History of the Development of Sulfanilamide (Para Amino Benzene Sulfonamide), *Proc. Staff Meet., Mayo Clin.* **13**:53-60 (Jan. 26) 1938.

Helmholz⁶⁹ stated that mandelic acid and sulfanilamide are two valuable drugs which have been made available during the past few years for the treatment of urinary infections. Mandelic acid is dependent for its action on a concentration in the urine greater than 0.5 per cent and a p_H of the urine less than 5.5, so that it is not likely to be successful unless the function of the kidney is normal or nearly so. If the urine does not reach the necessary p_H of 5.5, ammonium nitrate may be given in addition. The usual adult dose of ammonium mandelate is 12 Gm. daily. The output of urine in twenty-four hours should be kept at approximately 1,000 cc. Acidification of urine can be tested by the patient with the use of chlorphenol red. Proper acidity is indicated by yellow and insufficient acidity by red. It may also be tested by nitrazine paper, and the proper acidity is indicated by yellow. Insufficient acidity is indicated by green.

Mandelic acid is effective against all the common gram-negative bacilli, against *Staphylococcus aureus* and against *Streptococcus faecalis*. It is less useful in the treatment of infections caused by urea-splitting organisms, such as those of the *Proteus* group.

Helmholz has demonstrated that with sulfanilamide in concentrations easily obtainable by oral administration of the drug the urine is bactericidal for *Staph. aureus*, *Escherichia coli*, *Aerobacter aerogenes* and organisms of the *Proteus* and *Pseudomonas* groups. It does not, however, destroy *Str. faecalis*. Sulfanilamide is more effective in alkaline than in acid urine. This is of definite significance in the treatment of infections with *Proteus*.

Helmholz reported 2 cases of infection caused by *Esch. coli* and *A. aerogenes* respectively in which the infection yielded rapidly to administration of sulfanilamide after long and unsuccessful treatment with mandelic acid. The author concluded that sulfanilamide is the remedy of choice in the average case because of its ease of administration, its tolerance by the stomach and the fact that it can be used during the acute stage of the disease. It should not be used in the treatment of infections caused by *Str. faecalis*. Mandelic acid and sulfanilamide are used satisfactorily to supplement each other. The dose of sulfanilamide is 5 to 10 grains (0.32 to 0.65 Gm.) a day for infants and 20 to 30 grains (1.29 to 1.94 Gm.) a day for children 8 to 12 years of age.

ROENTGENOLOGY IN UROLOGY

Junker⁷⁰ described the results of his new method of roentgenologic diagnosis for surgical diseases of the kidney. He adapted to urologic

69. Helmholz, H. F.: A Comparison of Mandelic Acid and Sulfanilamide as Urinary Antiseptics, *J. A. M. A.* **109**:1039-1041 (Sept. 25) 1937.

70. Junker, H.: Fortschritte der chirurgischen Nierendiagnostik, *Ztschr. f. Urol.* **32**:112-128 and 191-207, 1938.

practice Berg's method of roentgenologic diagnosis of gastric lesions. After intravenous injection of skiodan a preliminary roentgenogram is made, and subsequently a series of roentgenograms of interesting details. This method offers striking advantages over ordinary pyelographic or pyeloscopic examination in detection of small but important changes. Anatomic changes of the calices, dysfunction of peristalsis in the calices and ureters, early changes in cases of tuberculosis and ascending pyelitis and the anatomic substratum of "essential" hematuria can be demonstrated clearly.

Excretory urograms of 27 normal pregnant women throughout the succeeding months of gestation and the puerperium showed varying degrees of dilatation of one or both ureters and renal pelves in every patient. The right kidney was more affected than the left, dilation of the ureter always began at the pelvic brim, and the pelvic portion was never significantly involved. The dilatation was progressive, reached its maximum several weeks ante partum and had disappeared by about the twenty-eighth day post partum. It occurred later (but was more severe) in primiparas than in multiparas. These findings were confirmed by anatomic and histologic studies of 13 parturient women, all but 2 of whom died at term.

In addition to dilatation of the ureters, great hypertrophy of the sheaths of Waldeyer at their lower ends was noted. There was a softening process in the wall of the abdominal portion of the ureter, the structure becoming flaccid and easily compressible. The growing uterus impinges on the ureter at the pelvic brim, especially the right, because its course over the iliac vessels differs from that on the left and makes it more susceptible to pressure. The dilatation which results can be diminished by the use of indwelling ureteral catheters if they are left in place longer than twenty-four hours. With the advance of pregnancy the excretion time of the kidney was greatly delayed, and lack of tone and decrease in rhythmic expulsive force of the dilated ureter were observed.

Hormonal activity contributes to the process of softening and atony of the ureter, which makes it susceptible to dilation from slight pressure.

A careful bacteriologic study of the urinary tracts of pregnant women as compared with those of nonpregnant women showed only a slight increase in the incidence of bacteria in the urine in the former.

Among 50 normal pregnant women, cultures of the urine from the bladder on brain broth mediums yielded bacteria in 64 per cent of cases, and cultures on blood agar mediums, in 36 per cent. Among 50 normal nonpregnant women, cultures yielded bacteria on brain broth mediums in 44 per cent and on blood agar mediums in 18 per cent of cases. Only 4 cultures yielding bacteria were obtained from the urine taken from the kidney among the 50 normal pregnant women.

Hundley's⁷¹ analysis of 236 patients with inflammatory disease of the urinary tract admitted to the obstetric wards of the Maryland University Hospital showed that 136 were primiparas and 100 multiparas. The symptoms were more severe among the primiparas. The incidence of pyelitis of pregnancy was 3.1 per cent. Confirming the observation that pressure changes in the urinary tract are not observed until after the sixteenth week, only 11 patients had pyelitis during the first four months of pregnancy. The frequency increases as pregnancy advances. In the middle trimester there were 32 cases; in the last period, 97; and post partum, 96. Twenty patients were delivered spontaneously, whereas in 11 cases pregnancy was interrupted artificially.

Treatment consists of medicinal, or palliative, measures and operative, or radical measures. Of Hundley's 236 patients, all but 25 responded to palliative measures, such as increased intake of fluid, postural treatment, administration of urinary antiseptics, such as mandelic acid and sulfanilamide, and the ketogenic diet. The last-mentioned drug has been abandoned because it produces a great decrease in the carbon dioxide-combining power of the blood and involves a restriction of fluids.

Hundley's experience with mandelic acid has been disappointing, and he has been conservative in the use of sulfanilamide until more definite proof is available as to its harmlessness in pregnancy.

If after six or seven days of medicinal treatment the symptoms are not alleviated, cystoscopic and ureteral catheterization are performed and are repeated as often as necessary. If the response to simple catheterization is not satisfactory, the ureteral catheters are left in place for twenty-four to forty-eight hours, but not longer, because they are likely to induce labor. In 11 cases in this series it was necessary to empty the uterus.

UREMIA

Wear, Sisk and Trinkle⁷² made an experimental and clinical study of peritoneal lavage in the treatment of uremia. With few exceptions, previous investigators have used saline solutions, dextrose solutions or a combination of these. The objectionable feature was that they removed not only nitrogenous elements but also such vital substances as calcium, chlorides and sugar. For this reason, Wear, Sisk and Trinkle chose lactate-Ringer solution for their first perfusion fluid.

71. Hundley, J. M.; Siegel, I. A.; Hachtel, F. W., and Dumler, J. C.: Some Physiological and Pathological Observations on the Urinary Tract During Pregnancy, *Surg., Gynec. & Obst.* **66**:360-379 (Feb.) 1938.

72. Wear, J. B.; Sisk, I. R., and Trinkle, A. J.: Peritoneal Lavage in the Treatment of Uremia: An Experimental and Clinical Study, *J. Urol.* **39**:53-62 (Jan.) 1938.

The procedure was carried out with the patient under morphine and pentobarbital sodium anesthesia. For continuous perfusion two trocars were used. A standard gallbladder trocar was introduced in the upper portion of the abdomen. The trocar introduced into the lower portion of the abdomen was modified by the placing of numerous small holes in its distal third to avoid occlusion of a single opening by the omentum and intestines. From an insulated reservoir the fluid was introduced into the upper cannula. The lower cannula was attached to rubber tubing which hung dependent into a bottle on the floor and acted as a siphon. The perfusion fluid was kept at a temperature of 40 C. in a water bath. Specimens of blood were taken before and after the lavage, and specimens were taken from the fluid recovered from the lavage.

Decrease in concentration of nonprotein nitrogen of the blood after lavage ranged from 10 to 59 mg. per hundred cubic centimeters. The greatest reduction occurred in cases in which the highest retention of nitrogen was present.

Wear, Sisk and Trinkle stated that they do not offer peritoneal lavage as a treatment for patients who have hopelessly damaged kidneys, but they feel that it is a method well worthy of trial in cases in which there is some hope of return of renal function. The procedure itself is without morbidity or mortality, and large quantities of nonprotein nitrogen can be removed. The treatment of uremia by this method is the treatment of a secondary damaging factor. Every effort should be made to combat the severe decrease in the carbon dioxide-combining power of the blood which is a rather constant and dangerous result of uremia.

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CRANIAL VENOUS SINUSES

CORRELATION BETWEEN ROENTGENOGRAMS OF THE OCCIPITAL BONE
AND THE QUECKENSTEDT (TOBEY-AYER) TEST

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It has been demonstrated previously that roentgenographic evidence of the relative volumes of the lateral sinuses corresponds to comparative anatomic evidence of the bony markings on the occipital bone.¹ The value of a clinical method for the demonstration of comparative volumes of the lateral sinuses has been briefly discussed in the presentation of that evidence. In order to elucidate further the relation between the actual volume of a sinus and a roentgenographic presentation of that volume, it appeared desirable to compare the responses of the internal jugular veins obtained during the performance of the Tobey-Ayer test with the roentgenographic picture of the markings of the lateral sinuses on the occipital bone of the same person. Since the result of the Tobey-Ayer application of the Queckenstedt test is directly influenced by the caliber of the major efferent cranial vessels, the presence of a favorable correlation should further indicate the clinical value of such roentgenograms.

For the purpose of this study, manometric investigations of the dynamics of the normal spinal fluid were performed on 100 patients in the general surgical wards of the Johns Hopkins Hospital. The original technic was used, and the qualifying factors noted by the originators of the Tobey-Ayer test² were taken into account. The response of the spinal fluid pressure to compression of the internal jugular vein on

From the Department of Surgery and the Department of Roentgenology, Johns Hopkins Hospital.

1. Woodhall, B.: Variations of the Cranial Venous Sinuses in the Region of the Torcular Herophili, *Arch. Surg.* **33**:297-314 (Aug.) 1936. Woodhall, B., and Seeds, A. E.: Cranial Venous Sinuses: Correlation Between Skull Markings and Roentgenograms of the Occipital Bone, *ibid.* **33**:867-875 (Nov.) 1936.

2. Tobey, G. L., Jr., and Ayer, J. B.: Dynamic Studies on the Cerebrospinal Fluid in the Differential Diagnosis of Lateral Sinus Thrombosis, *Arch. Otolaryng.* **2**:50-57 (July) 1925.

either side, the speed of the response on application of the compression and on its release and the response to simultaneous compression of the

COMPILATION OF RESULTS

Interpretation of Roentgenograms	No.	Findings on Performance of Tobey-Ayer Test	No.
1. Right lateral sinus greater than left		Response of right internal jugular vein greater than that of left.....	5
Slight difference.....	11	Responses equal	6
Moderate difference.....	5	Response of right internal jugular vein greater than that of left.....	5
Pronounced difference.....	6	Response of right internal jugular vein greater than that of left.....	6
	<hr/> 22		<hr/> 22
2. Right lateral sinus visible; no left....	5	Response of right internal jugular vein present; little if any response of left internal jugular vein.....	4
		Response of right internal jugular vein greater than that of left.....	1
			<hr/> 5
3. Left lateral sinus greater than right		Response of left internal jugular vein greater than that of right.....	6
Slight difference.....	11	Responses equal	5
Moderate difference.....	3	Response of left internal jugular vein greater than that of right.....	3
	<hr/> 14		<hr/> 14
4. Left lateral sinus visible; no right....	3	Response of left internal jugular vein present; little if any response of right internal jugular vein.....	2
		Response of left internal jugular vein greater than that of right.....	1
			<hr/> 3
5. Both lateral sinuses visible and of equal volume.....	40	Responses equal	23
		Response of right internal jugular vein slightly greater than that of left.....	10
		Response of left internal jugular vein slightly greater than that of right....	2
			<hr/> 40
6. Indistinct markings.....	16	Responses equal	12
		Response of right internal jugular vein greater than that of left.....	2
		Response of left internal jugular vein greater than that of right.....	2
			<hr/> 16

RÉSUMÉ

Roentgenograms	No.	Tobey-Ayer Tests	No
Right lateral sinus greater than left....	22	Response of right internal jugular vein greater than that of left.....	29
Right lateral sinus visible; no left.....	5	Response of right internal jugular vein present; no response of left.....	4
Left lateral sinus greater than right....	14	Response of left internal jugular vein greater than that of right.....	14
Left lateral sinus visible; no right.....	3	Response of left internal jugular vein greater than that of right.....	2
Both lateral sinuses visible and of equal volume.....	40	Responses equal	51
Indistinct markings.....	16		<hr/> 109
	<hr/> 100		

internal jugular veins were recorded, frequently by means of a simple tambour and sphygmograph. After the completion of each manometric

study, roentgenograms of the occipital bone in the anteroposterior plane were taken for comparison.

COMMENT

This study of a second series of 100 roentgenograms of the occipital bone of persons on whom precise manometric studies of the dynamics

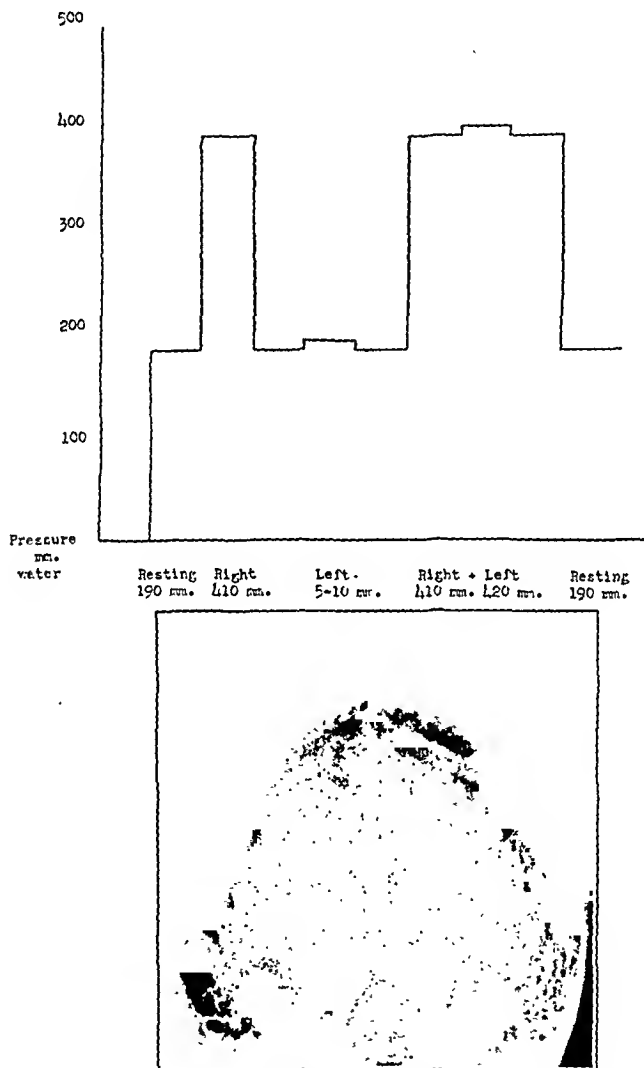


Fig. 1.—*A*, diagram of the response to the Queckenstedt (Tobey-Ayer) test of a patient with a unilateral cranial sinus pattern. *B*, cranial roentgenogram of the same patient. Markings of the right lateral sinus are visible. No markings of the left lateral sinus are visible.

of the normal spinal fluid have been made by the method of Tobey and Ayer indicates again that such roentgenograms may be considered a

reliable index of the volume of the lateral sinuses. In the relatively low percentage of cases in which the markings of the lateral sinuses are not distinct in the occipital projection, roentgenographic study of the base of the skull, with visualization of the size of the jugular foramens, may

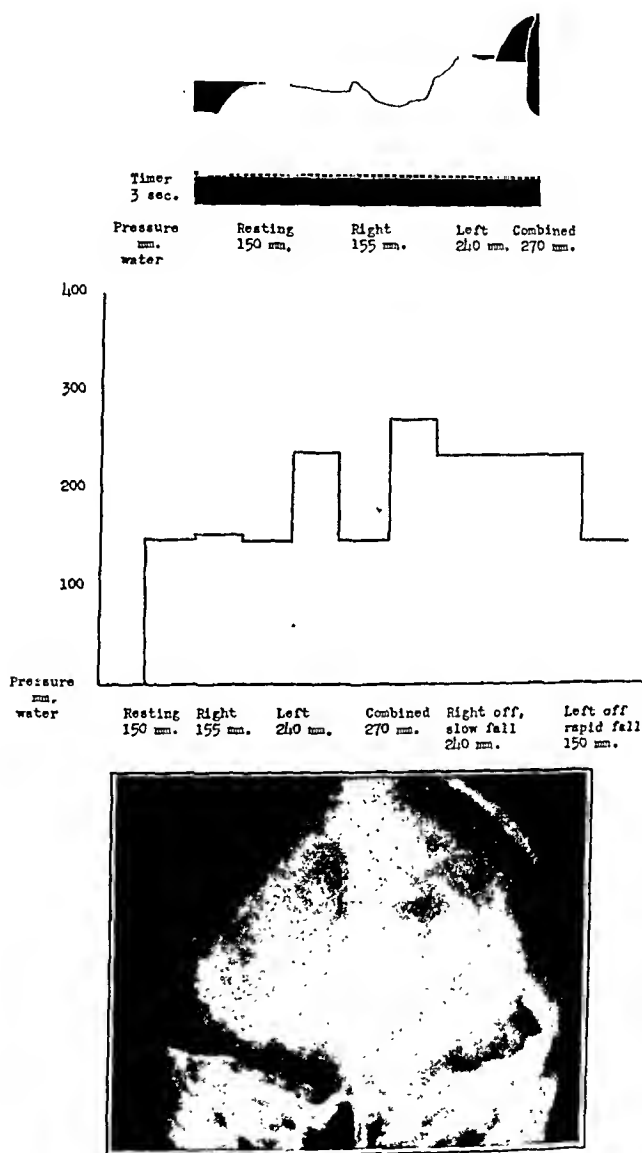


Fig. 2.—*A*, kymographic record of a positive response to the Tobey-Ayer test on compression of the right internal jugular vein. The response was negative, or normal, on compression of the left internal jugular vein. *B*, diagram of response to the Tobey-Ayer test for a patient with a unilateral cranial sinus pattern. *C*, cranial roentgenogram of the same patient. Markings of the left lateral sinus are visible. No markings of the right lateral sinus are visible.

Timer
 3 sec.
 Pressure
 mm.
 water

Resting	Left	Right	Combined
100 mm.	150 mm.	145 mm.	240 mm.



Fig. 3.—*A*, kymographic record of a patient with a bilateral and equal response to the Queckenstedt (Tobey-Ayer) test. *B*, cranial roentgenogram of the same patient, showing markings of bilateral and equal sinuses.

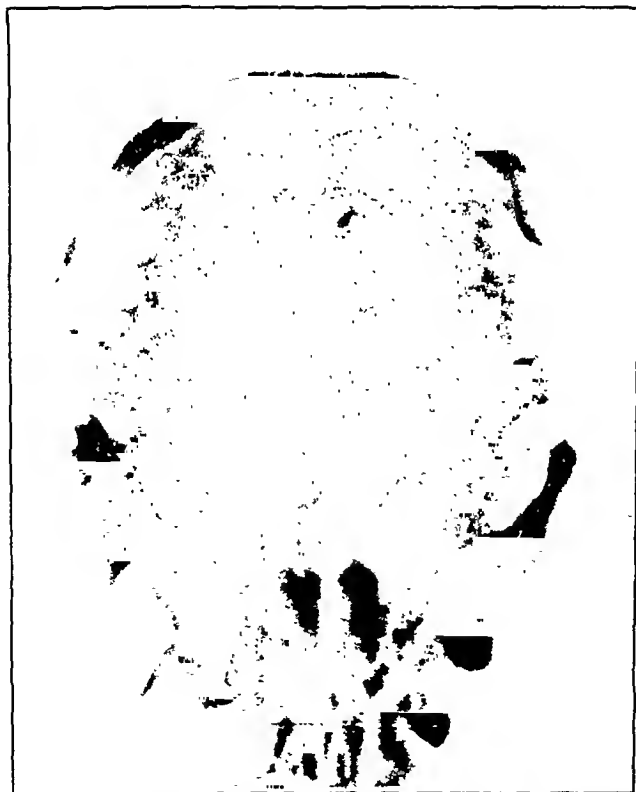


Fig. 4.—Cranial roentgenogram of a patient in whom the right jugular foramen was larger than the left.

be substituted. Although a statistical study has not as yet been completed of the latter projection, it is evident that a combined occipito-basilar visualization of the markings of the lateral sinuses and of the jugular foramens should provide complete roentgenographic evidence of the comparative volumes of these major efferent cranial vessels.

EVOLUTION OF TREATMENT OF FRACTURE OF NECK OF FEMUR

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MONTCLAIR, N. J.

The purpose of this article is to present an account of the evolution of the treatment of fractures of the neck of the femur, more specifically of those of the transcervical type.

In the exhaustive survey made toward this end I have tried to take up the various methods in chronologic order as much as possible. In a few exceptional cases, as in the discussion of the open treatment of these fractures, I have found it necessary to deviate from the general plan mentioned.

Of all the fractures with which the surgeon has had to deal, it is generally conceded that the one that has given him the most trouble and disappointment is the fracture of the hip. Until recently the best that he could expect to promise was bony union and a cure in about 1 out of 3 cases. While a similar state of affairs formerly obtained for fractures of the patella, the carpal scaphoid and the olecranon, at present the improved methods of treatment of these fractures have surmounted the dangers of failure of bony union. There remains, therefore, only the problem of the fractured hip to contend with; and in the light of present day interest and progress in this field, the handicaps in treatment of this fracture likewise seem doomed, and success appears on the horizon.

Up to the present time, with only such a poor prognosis to offer, namely, bony union in 1 of 3 cases, the surgeon's attitude and approach toward new cases have not been happy. It has been stated that in some of the very large, active hospitals patients with such fractures were refused admittance because they occupied limited bed space futilely and for such prolonged periods. Since so little could be done for them at the hospital, it was thought that they should be cared for at home.

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The illustrations for this article have been taken from other publications. In each instance the name of the author is given in parentheses at the end of the legend, and the complete reference to the source appears under the author's name in the bibliography.

The method of treatment of such fractures has been constantly changing because of all too frequent failures. I shall therefore endeavor to trace the history of their treatment from the time of the earliest recorded case, with its feeble and profoundly inadequate management, through the period during which various types of crude and uncomfortable splints were used, to a period when the condition was generally regarded as hopeless and nothing but conservative methods were applied, such as the placing of a pillow under the knee; then on through a period of more or less inactivity until the plaster of paris abduction treatment became the vogue; and finally, as surgery became more highly perfected, to the period of introduction of the more radical methods of internal fixation used at the present time. The last-mentioned methods seem unquestionably to have opened up a new avenue in this field, and because of the remarkably successful results reported to date they promise to be regarded as the greatest advance made in orthopedic surgery in the last quarter of a century.

During the compilation of the data for this historical survey, I could not but be impressed by the emphasis placed (rightly) by our predecessors on the anatomic, pathologic, mechanical and clinical aspects of the condition as applied to its treatment. A proper consideration of the anatomy of the hip joint, the osseous structure of the neck of the femur, the classification of the types of fracture in this region, the displacements of the fragments and the cause, signs and symptoms of this fracture is therefore essential to a clearer understanding and evaluation of the early efforts made in its treatment.

DEFINITION AND CLASSIFICATION

Formerly fractures of the neck of the femur were classified as either intracapsular or extracapsular fractures, according to their location within or without the capsule of the hip joint. At present they are more accurately designated as subcapital (fig. 1) or near the head, transcervical or central, and basal, or near or through the base of the neck.

The fracture may also be impacted, incomplete, complete, oblique, transverse or comminuted. The fractures that appear impacted on roentgen examination often are those in which severe displacement is present, such as when the fragments occupy an end to side position. The roentgenograms in such cases are deceptive unless lateral views are taken. Rarely a true impacted fracture has been observed, in which case the patient was up and about with no immobilization applied. The incomplete and impacted ones occur more often at the base, while the complete fracture is found in the proximal or central regions. The comminuted type usually is produced by a direct fall on the greater

trochanter. The prognosis is better in such cases, because of the greater amount of force required to fracture the bone, than it usually is for the senile patient.

ETIOLOGY

Fracture of the neck of the femur usually occurs in persons over 50 years of age. There is a slight predominance of women over men.

Owing to the fact that the fracture commonly occurs in the aged, in whom degenerative changes in the neck of the femur are frequently found, such as absorption and rarefaction of bone, the ease with which this fracture follows trauma may well be imagined. Some authorities go so far as to state that often it is a slight sudden twist of the leg, occurring, for instance, as the result of getting the toe of the shoe

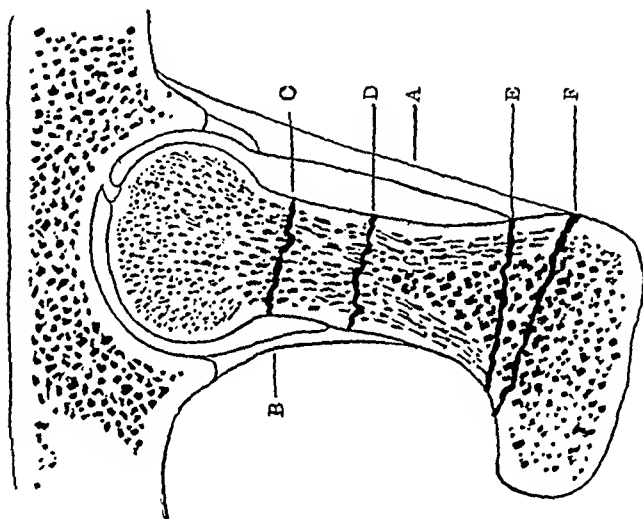


Fig. 1.—Sites of fracture. (From Wilson and Cochrane.)

caught on a rug or against a rough pavement or curbstone, that actually causes the fracture and that the fall that takes place is a result rather than the cause of the injury. A direct fall on the feet from a height or a fall on the trochanter may also produce this fracture. This is more often the case with younger or middle-aged persons, in whom osteoporotic changes in the neck of the femur are not yet present.

CLINICAL SIGNS

The typical picture of a patient with fracture of the neck of the femur is that of an aged person lying in the supine position with the affected leg apparently helpless and rolled outward, so that the outer border of the foot is lying on the pavement or floor. Slight adduction of the limb is noted. On comparative measurement of both legs, the affected one shows shortening. The iliotibial band is found to be

relaxed. There is local tenderness over the greater trochanter. The tip of the greater trochanter lies above Nélaton's line, a line drawn from the anterior superior spine of the ilium to the tuberosity of the ischium. The base of Bryant's triangle is shortened. This is determined with the patient lying on his back. One side of the triangle is a perpendicular from the anterior spine to the table, and the other side is one joining the anterior superior spine of the ilium and the tip of the greater trochanter. The base is a line running horizontally from the tip of the greater trochanter to the perpendicular line. The roentgen findings are essential for the final diagnosis and for determining the type of fracture.

ANATOMY OF THE HIP JOINT

The hip joint is a ball and socket joint composed of the cup-shaped acetabulum and the almost spherical head of the femur. The strong capsular ligaments and the teres ligament enclose the joint and maintain it in place. The capsular ligaments are attached to the rim of the acetabulum and to the anterior and posterior intertrochanteric lines of the femur, incorporating the major portion of the neck of the femur within the capsular joint space.

The acetabulum is a large cup-shaped cavity on the lateral aspect of the hip bone. The lower part is deficient, and the gap is called the acetabular notch; a fibrous band called the transverse ligament fills in this gap.

The upper end of the femur is made up of the head, the neck and the greater and lesser trochanters. The head, which is rounded and forms more than a hemisphere, is directed upward, inward and a little forward. There is an ovoid depression, the fovea, on its smooth surface just below and behind the center, to which the ligamentum teres is attached.

The neck is the thick bar that connects the head with the body in the region of the trochanters. It is nearly 2 inches (5 cm.) long, is thinnest in the middle and is widest toward each end, especially the end which joins the body. The neck joins the body at an obtuse angle of 125 to 135 degrees. The obliquity of the neck varies with the age of the person and ranges from a gentle curve in infancy to almost a right angle in old age.

The greater trochanter is the large square prominence on the lateral aspect of the femur, where the neck joins the shaft. Its root is marked off from the shaft by a more or less horizontal ridge on its lateral aspect, called the vasternus line. The powerful outward rotator muscles of the thigh are attached to the greater trochanter.

The lesser trochanter is the rounded conical projection on the posterior and medial aspect of the bone, where the lower part of the neck joins the body.

The anterior intertrochanteric line is the rough broad line which extends from the upper part of the anterior surface of the greater trochanter toward the lesser trochanter. The posterior intertrochanteric line connects the upper and back part of the lesser trochanter on the posterior surface of the neck of the femur.

The head is covered with cartilage and so is the acetabulum, with the exception of the depressions found in both for the attachment of the teres ligament. A mass of fat covered with synovial membrane occupies the acetabular notch.

The capsular ligament (figs. 3 and 4) of the hip joint, a strong, dense ligamentous capsule, is made up of three portions: the iliofemoral, pubofemoral and ischiocapsular ligaments. It is attached at the brim of the acetabulum above; below, it is attached in front to the femur along the anterior intertrochanteric line, above to the neck a little short of its junction to the greater trochanter, behind to the neck itself about $\frac{1}{2}$ inch (1.3 cm.) from the posterior intertrochanteric line, and below to the upper part of the lesser trochanter.

Thus there is formed a sort of tubular sheath embracing the hip joint. It consists of two sets of fibers, circular and longitudinal. The circular fibers, the zona orbicularis, are most abundant at the lower and back part of the capsule and form a sling or collar around the neck of the femur. The longitudinal fibers are most numerous at the upper and front part of the capsule, where they form distinct bands or accessory ligaments, of which the most important is the iliofemoral ligament. Other accessory bands are the pubofemoral and ischiocapsular ligaments.

The ligamentum teres is a triangular band the apex of which is inserted into the depression in the head of the femur, and its broad base takes origin in the margins of the acetabular notch, becoming blended with the transverse ligament that bridges this notch. It runs upward from the acetabular notch to the head of the femur. It consists of connective tissue, surrounded by a tubular sheath of synovial membrane. Sometimes only the synovial fold exists. The ligamentum teres on rare occasions may be absent.

Circulation.—The circulation (fig. 5) to the hip joint is derived from the circumflex artery of the profunda femoris, the external circumflex and the superficial circumflex iliac of the femoral artery. According to Kolodny, there are four sets of blood vessels to the head and neck of the femur: 1. Vessels from the shaft, which enter from the superior nutrient artery and through the neck to the head; (2) periosteal vessels, which pass superficially along the borders of the neck into the head (as the existence of periosteum on the neck of the femur is disputed, these vessels should probably be called, according to W. C. Campbell, synovial, as they must pass in the synovial membrane which is reflected

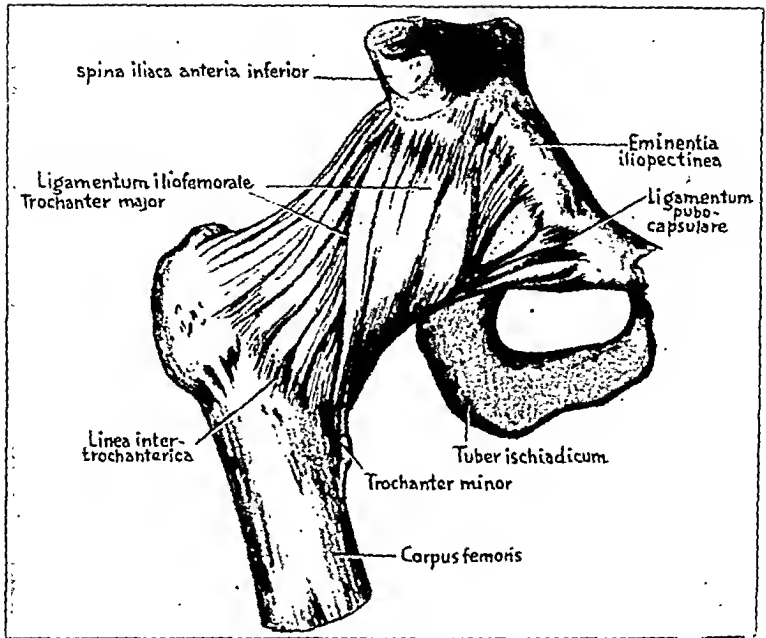


Fig. 3.¹—Drawing of the hip, anterior view, showing the ligaments. The ligamentum iliofemorale, or Y ligament, is prominent. (From Campbell.)

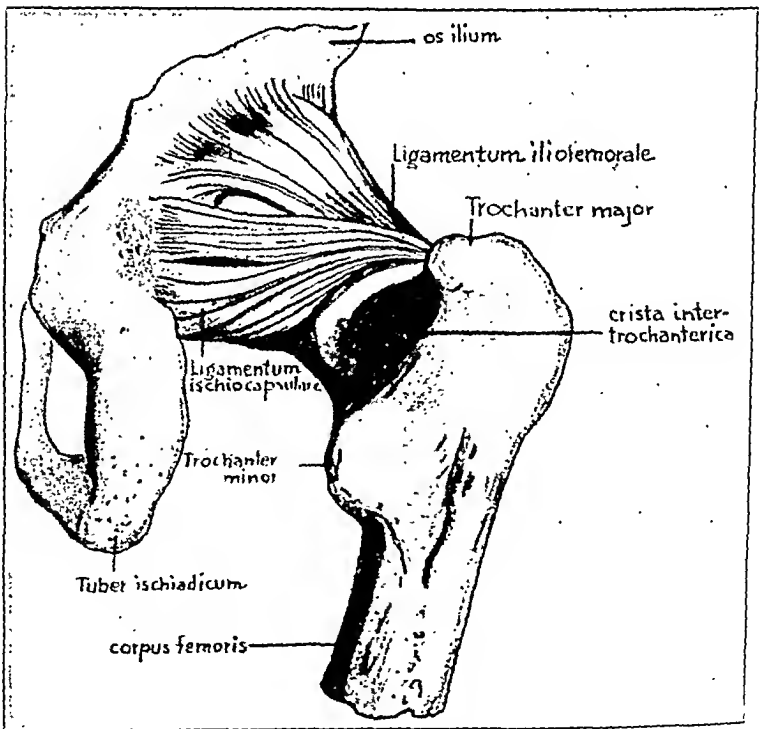


Fig. 4.—Drawing of the hip, posterior view, showing the ligaments, including the ischiocapsular and ischiofemoral ligaments. A considerable portion of the posterior aspect of the extracapsular portion of the femoral neck is also shown. (From Campbell.)

1. Figure 2 has been omitted.

over the neck); (3) epiphysial vessels, which pass to the epiphysis from the capsule, and (4) vessels from the ligamentum teres, which enter the head at the depressed area known as the fovea.

W. E. Wolcott preferred to designate the circulation of the hip joint as consisting of a threefold blood supply: (1) ligamentum teres artery, (2) posterior superior visceral capsular arteries and (3) posterior inferior visceral capsular arteries.

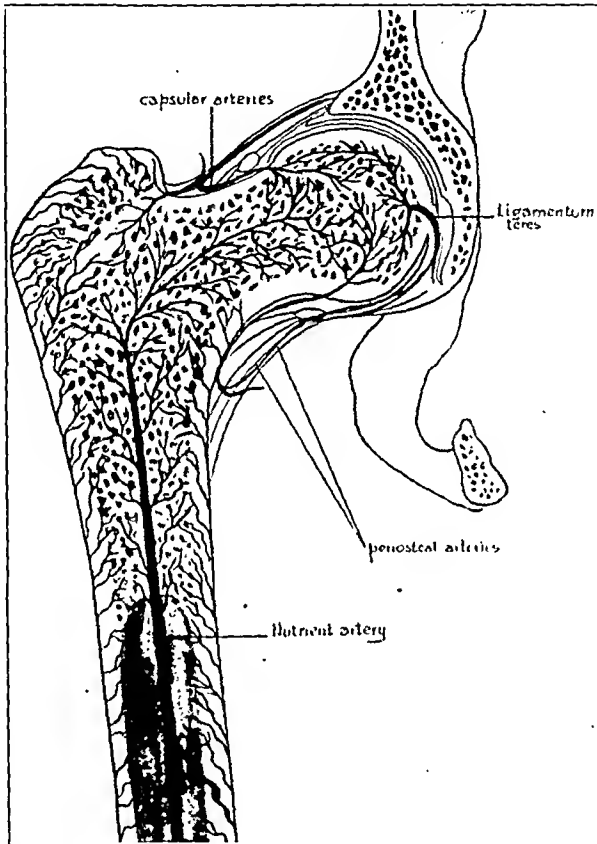


Fig. 5.—Schematic drawing showing circulation to the head and the neck of the femur. (From Campbell.)

Muscle Action.—The muscles which flex the femur on the pelvis are the iliopsoas, the rectus femoris, the sartorius, the pectineus, the adductor longus, the adductor brevis, the anterior fibers of the gluteus medius and the gluteus minimus.

Extension at the hip joint is mainly performed by the gluteus maximus assisted by the hamstrings.

The thigh is adducted by the adductor magnus, the adductor longus, the adductor brevis, the pectineus, the gracilis and the lower and upper parts of the gluteus maximus.

The muscles which rotate the thigh inward are the anterior fibers of the gluteus medius, the gluteus minimus and the tensor fasciae femoris; those which rotate it outward are the posterior fibers of the gluteus medius, the fibers of the piriformis, the obturator externus, the gemelli, the quadratus femoris, the iliopsoas, the gluteus maximus, the three adductors, the pectineus and the sartorius.

DISPLACEMENTS

The proximal or head fragment in intracapsular fracture of the neck of the femur possesses extreme mobility because of its smooth and lubricated surface, because of the presence of blood and synovial fluid, because of its position within a tube of capsule (even though this is torn, as frequently is the case) and because with the single exception of the ligamentum teres there is no other structure attached to it that might prevent its motion. The various positions that this fragment can assume in respect to that of the neck fragment are therefore many.

The head fragment, then, can assume various positions in respect to the neck fragment. It may be tilted backward or in external rotation; forward, or in internal rotation; upward, or in flexion; downward, or in hyperextension; or it may remain in the neutral position, or normal extension. The commonest positions assumed by the head fragment, however, are forward tilt, upward and neutral. Displacements of the distal or neck fragment are largely due to muscular action and gravity. This fragment usually is pulled upward by the gluteal muscles, the iliopsoas muscle, the adductors and the hamstrings, causing shortening of the limb. It is also outwardly rotated by the powerful gluteal muscles, the piriformis and the gemelli. The force of gravity, because of the angle of the foot to the leg, also enters into the external rotation produced. Likewise, because of gravity, the distal or neck fragment is displaced backward, in relation to the patient's body.

Owing to all these influences, namely, the extreme mobility of the head fragment and the muscular and gravitational effects produced on the distal or neck fragment, the fractured surfaces of these fragments may assume various positions and relations to each other. These are as follows:

1. The open V position. In this position the head fragment is tilted forward and the neck fragment rotated outward, so that the posterior edge of the head fragment fracture surface is cocked on the fracture surface of the distal fragment.

2. The neutral position. The fracture surfaces are approximated to each other, probably with a little upward and backward displacement of the distal fragment. This often is the case in impacted fractures.

3. Placement of the fracture surface of the capital fragment behind the neck of the cervical fragment.

4. Placement of the fracture surface of the cervical fragment behind the capital fragment.

HISTORY OF TREATMENT

Historically, the great battlefield in fracture surgery has been the fractured hip. The results obtained in the treatment of fracture of the neck of the femur have been far from satisfactory. Numerous methods of treatment have been tried and discarded after their failure has been demonstrated. After the fracture had been reduced, how was it to be kept successfully immobilized, so that nature could be given a chance to heal it? On account of this difficulty one prominent surgeon of the present time has gone so far as to call it the "unsolved fracture."

In this historical survey I shall be concerned mainly with the methods that have been attempted for reduction and for securing immobilization of the fracture.

AMBROISE PARÉ: THE FIRST RECORDED CASE

It is not known for certain whether the ancients had knowledge of the existence of fractures of the neck of the femur. Boyer has stated that, "Although Hippocrates has not, in the exact words, spoken of this fracture there can be no doubt, from several passages in his article on fractures of the thigh-bone, that he had seen it." Malgaigne likewise credited the ancients with positive knowledge of this condition. The first report, however, that has been recorded in the literature is that of Ambroise Paré (1510-1590) in his "Works of Ambroise Paré." This epoch-making report is as follows:

A fracture sometimes happens at the joint of the hip in the neck of the thigh bone, as I once observed in an honest matron. I being called to her, when I had observed the hurt thigh to be shorter than the whole, with the outward prominence of the ischium, which at the first sight I supposed to proceed from the head of the thigh bone, I presently persuaded myself it was a dislocation. I then therefore extended the bone, and forced (as I thought) the head thereof into its cavities. The equalities of both the legs in bigness which followed upon this extension, increased my persuasion that it was a dislocation. The next day I visited her the second time, and found her in great pain, her hurt leg shorter, and her foot rested inwards. Then I loosed all her ligatures and perceived such a prominence as I did formerly. Wherefore I endeavored again to force in the head of the bone, as I formerly did. But as I was busied therein, I heard a little crackling and also I considered that there was no cavity or depression in the joint, by which signs I certainly persuaded myself that the bone was broken and not dislocated. Neither only such kind of fractures, but also the separation of the appendix or head of this bone from its place, may induce one to think it a dislocation; which thing has sometimes deceived some heedless surgeons, who have not dreamt of the divulsion or separation of the appendix from the top of the thigh-bone but have judged it only a dislocation.

Then, therefore, I set the bone, and joined the fragments together, laid thereupon splints (fig. 6) with compresses, made ligations with a rowler, having two heads wrapped about the joint, and the body crosswise, and I defended her foote with a case, that none of the clothes might press it. I fastened a rope to a post, and so let it come down into the midst of the bed and tied therein many knots, for the better taking hold and lifting up herself.

Thus, Ambroise Paré became the first to recognize and report a case of fracture of the neck of the femur. Morgagni (1682-1731) was the next. Heister (1683-1758) and Ruysch (1638-1731) described the pathologic appearance of this fracture as observed at autopsy and were definite in their assertions that Paré deserved the credit for first recog-

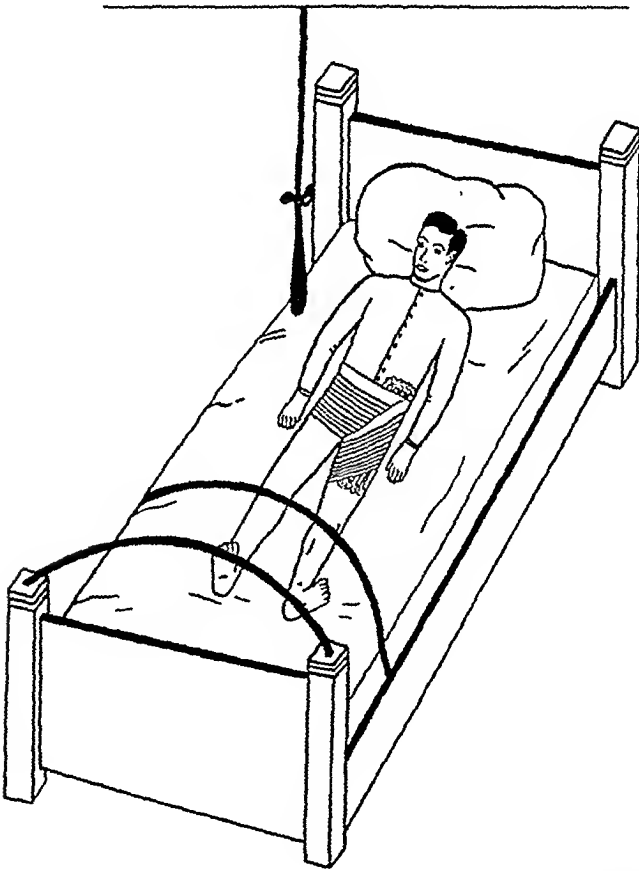


Fig. 6.—Ambroise Paré's method. A compress and splints are applied to the affected hip with a spica inguinalis bandage over all, a rope suspended from the ceiling and a cradle provided for protection of the feet. (From Hindinarst.)

nizing it. Later, Petit, Henry Earle, John Bell and others likewise looked on Paré as the pioneer in this field.

The treatment employed by Ambroise Paré consisted simply of compresses applied about the hip joint with splints and a spica inguinalis bandage over all.

This method, then, the crudity and inefficiency of which are so apparent, constitutes the first method of treating a fracture of the neck of the femur of which record is found in the literature.

The next method was that of Fabricius Hildanus (1537-1619). It was called the girt or belt of Hildanus (fig. 7) and consisted of a "belt drawn and buckled very tightly above the knee, the belt being first introduced through the eyes of two hooks," one on the outer and the other on the inner aspect of the knee. The ends of a rope were attached to these hooks. A double pulley was attached to the middle of this rope, and another pulley was tied to the eye of a screw made fast to the foot of the bed. A series of ropes was passed through, connecting both pulleys with the free end used to modify the amount of extension applied to the leg.

Counterextension was obtained by the use of two sheets which acted as perineal bands and were attached to each side of the headposts of the bed.

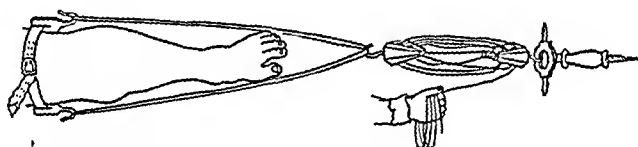


Fig. 7.—Girt of Hildanus. Traction is produced by means of a system of pulleys attached on one side to a rope which is anchored at the knee by two hooks and a circular strap above the knee and on the other side to a screw fastened to a wall of the room. (From Boyer.)

In the method of Hildanus one sees the principle, of extension and counterextension applied for the first time in the treatment of fracture of the neck of the femur.

Lawrence Heister (1683-1758) made use of this method, as described by him in his "System of Surgery," published in 1750.

Benjamin Gooch (?-1780) sought a better method than that of Hildanus by applying the principle of distention (fig. 8). He used a metal ring at the upper part of the thigh and one for the lower part, just above the knee. Two metal rods were fixed to the outer and inner parts of the upper ring and were shaped in the form of a screw at their lower ends. The lower ring had attached to it on each side an eye through which the screws of the side pieces worked. Then with a special screw key the side pieces could be lengthened as desired to get the effect of distention. For immobilization, a splint of thin timber was wrapped around the thigh and held in place by fillets.

Gooch attempted by this method to apply an old principle, known and employed by Hippocrates, namely, the principle of distention or distraction, such as was used for fracture of the shaft of the femur.

John Aitken (?-1790), of Edinburgh, improved on Gooch's machine by using a firm leather strap lined with soft flannel, applied around the pelvis (fig. 9). Three metal splints were attached to this strap and to a lower leather strap just above the knee by passing through three iron screw plates. They were fixed by screw nails passing through one of the holes at the lower end of the steel splints. Thus the length of the steel splint could be graduated as desired for distraction. A soft strap which was forked at its lower free end was fixed to the back part of the upper circular strap. The forked ends were brought around each side of the thigh and tied around the forepart of the circular strap to secure it from moving upward.

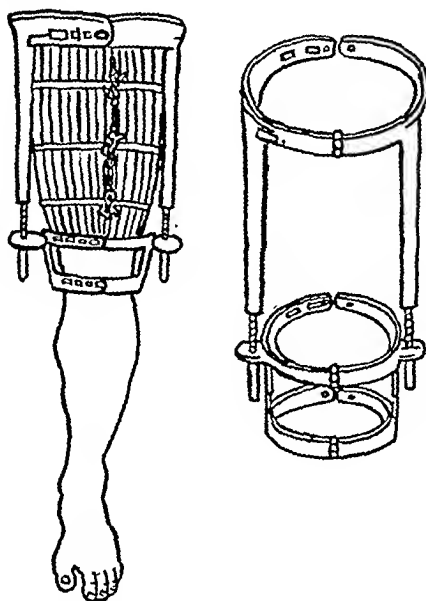


Fig. 8.—Gooch's machine, utilizing the principle of traction and countertraction by a process of "distention" or "distraction" regulated by the two screws at the lower ends of the side pieces. (From Boyer.)

Jean Louis Petit (1674-1750) described a case of fracture of the neck of the femur that he treated by means of extension and counter-extension. He obtained the latter by a sheet or perineal band across the groin of the sound hip and the former by two extension straps, one above the condyles of the knee and one above the malleoli. Each of the latter two straps was made fast to the foot of the bed, and they were used alternately for the convenience of the patient. A long outer junk or pasteboard splint from the crest of the ilium to beyond the foot and a shorter inner junk from the groin to beyond the foot were fastened to the leg by means of crosswise straps. A napkin drawn around the pelvis to fix the upper end of the long outer splint was applied. A sole fastened by a double strap served to keep the foot firm. A cord was

fastened to the ceiling, dropping to the middle of the bed within reach of the patient's hands to provide support.

The principle of extension and counterextension was employed as the sole method of treatment up to this point. The next method to be mentioned was exactly opposite, namely, treatment with the limb in semi-

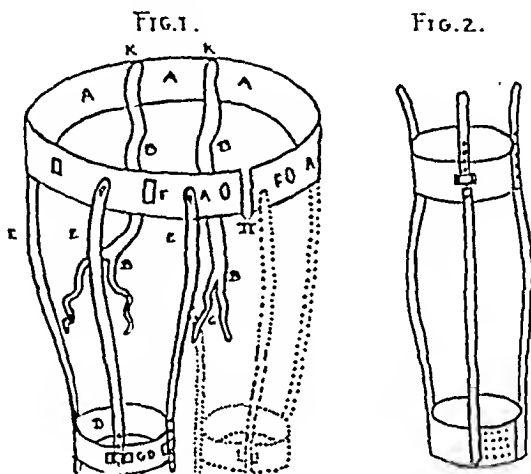


Fig. 9.—Aitkin's machine, operating on the same principle as the Gooch machine except that a waistband is substituted for the band in the groin. (From Boyer.)

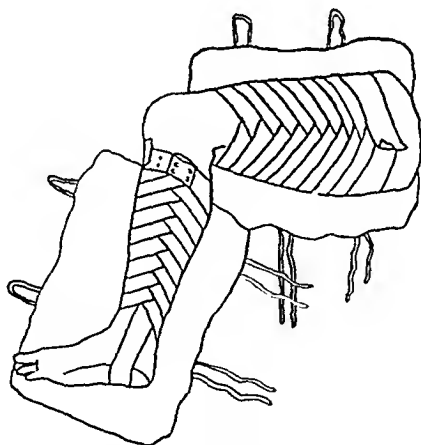


Fig. 10.—Percival Pott's method, utilizing the semiflexion position to relax the muscles and thus balance the forces on the osseous fragments at the site of fracture. (From Boyer.)

flexion. The great advocate, as well as the original proposer, of this position was Percival Pott (1713-1788), who was said to have worked a complete revolution in this department of surgery. Pott placed the patient on the affected side (fig. 10), with the plane through the anterior superior spines of the ilii perpendicular to the horizon, the thigh

drawn up to an obtuse angle with the pelvis and the leg bent to a right angle with the thigh. This position was believed by its originator to accomplish the effect of immobilization of the fragments and at the same time to prevent a displacement of the fragments at the fracture site by having the extensor and flexor muscles of the thigh in complete neutralization and balance.

While Pott's method itself did not become widespread in its use, it will be noted how his principles, semiflexion and muscular balance, were utilized again and again in other methods to be described later.

Desault (1744-1795) raised objections to this position on the grounds that (1) there was the difficulty of making extension necessary on the broken bone, (2) the impossibility of accurately comparing the two limbs, (3) the inconvenience of lying on the side, (4) the injurious pressure sustained on the greater trochanter, (5) the danger of derangements to which the fracture was liable when the patient went to stool and (6) the difficulty of firmly fixing the leg.

Desault therefore improvised a splint (fig. 11) which he believed obviated these difficulties. It returned to the principle of extension and counterextension. The description of the Desault splint is as follows:

A long flat wooden splint from the crest of the ilium to about 6 inches (15 cm.) beyond the foot was used as an outer splint. The lower end of the splint was notched and had a mortise to which the lower extending bandage around the leg was tied. A bandage was placed around the pelvis to secure this splint from being displaced upward; also, to aid in this respect, there was a bandage passing around the upper end of this splint and across the perineum, the tuberosity of the ischium acting as the anchoring support. An anterior splint from the groin to the knee was applied and held in place by four circular straps around the thigh, incorporating the external splint. Three circular straps maintained the latter splint to the leg. A figure of eight bandage around the foot was tied to the mortise in the notch at the lower end of the splint. Desault believed that this splint satisfied the three essential requirements for osseous union, namely, to keep the body of the femur down, to retain the pelvis up, and to secure the foot in a straight line with the leg as much as possible. Before the time of Desault, counterextension was made by a perineal band fastened to the headboard of the bed whereas Desault applied counterextension by means of his long "permanent extension" splint.

[NOTE.—Desault's wife suffered a fracture of the neck of the femur in 1830 and died of pneumonia after one month. Paradoxically, she was treated by use of the double inclined plane, the prevalent method of the day.]

PERIOD OF SIR ASTLEY COOPER

The next period was that of Sir Astley Cooper (1768-1841), who made the treatment of intracapsular fracture of the neck of the femur a subject of lively debate among his contemporaries. This period is considered by many authorities as that in which the first serious contributions on the nature and treatment of this condition were made. In fact, many of the recent articles dealing with the method of treatment of such fracture declare that the first rational treatment dates back to Sir Astley Cooper. He was the exponent of conservative treatment. This is very well described in his own words, which have been quoted frequently in the literature on this subject:

Not having found any mode of treatment succeed in effecting ossific union in these cases, and having repeatedly seen the patient's health much injured by the trials which have been made, all that I now direct to be done, is, that a pillow should be placed under the limb for its whole length, and a second rolled up, put under the knee, and that the limb should be allowed to remain upon these

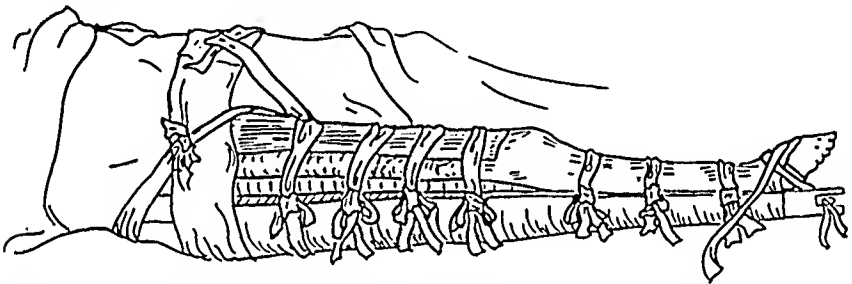


Fig. 11.—The Desault splint. A long side splint and a short anterior splint are used, and permanent traction is maintained by fixing the foot to a notch at the distal end of the long splint and anchoring the hip to the proximal end of this same splint. (From Boyer.)

for 10 days or a fortnight, until pain and inflammation have subsided; the patient should then be allowed to rise and sit in a high chair; to prevent much flexion of the limb, which would be painful, in a few days more he should begin to walk with crutches, and after a time, a stick should be substituted for the crutches, and in a few months he will be able to use the limb without any adventitious support; when he commences to bear the weight of the body on the limb he should be provided with a high heeled shoe which will much assist him.

Notable among Sir Astley Cooper's contributions to knowledge of this subject was his clear segregation of the fractures into two classes: (1) fractures through the neck proper ("intracapsular"), and (2) fractures through the trochanters ("extracapsular"). He was the first to bring out the importance of this fact and its bearing on the ultimate prognosis. In his time the outlook for fractures of the first type was extremely poor, while that for fractures of the second type was very good.

While Sir Astley Cooper claimed that bony union was difficult to obtain for "intracapsular" or transcervical fractures because of want of proper apposition, adequate lateral pressure on the fragments and deficient nutrition of the parts due to severance of the articular capsule, he did not deny the possibility of osseous union; "if a fracture should happen without the reflected ligament being torn, nutrition would continue and the bones might unite."

Therefore, Cooper was primarily interested in saving life rather than in obtaining osseous union at the site of fracture. But this conservative attitude did not go unchallenged; in fact, the feeling in the opposing camp, composed of Dupuytren, Boyer, Malgaigne, Charles Bell, Henry Earle and others, was strongly in favor of the belief that osseous union was possible and therefore that efforts should be made toward positive and deliberate treatment to attain this end.

Philip Physick (1768-1867) modified Desault's method by increasing the length of the outer splint to reach the axilla of the affected side. The splint ended in a crutchlike form for comfort in the axilla. The counterextension band was made to go from the perineum to a mortise-hole in the splint, high up near the axilla.

To keep the foot from being pulled outward and pressed against the external splint, Hutchinson modified Physick's splint by attaching a wooden block to the inner aspect of the lower end of the external splint. The extending band around the foot and ankle was then made to go across the inner, or free, end of this block of wood, thus keeping the foot from pressing against the external splint.

Dupuytren (1777-1835) objected to Desault's splint because the external splint caused pressure necrosis of the soft tissues over the greater trochanter and pain at the hip. These objections, he stated, often necessitated removal of the apparatus, and shortening of the leg would follow. This occurred in the case of General Lafayette. (Mention is made of this case only because of its historical interest.)

His mode of treatment consisted first in reducing the fracture by flexing the thigh on the abdomen and the leg on the thigh and then "drawing the thigh from the abdomen." This caused the limb to overcome the shortening and assume its natural length and the foot to correct its eversion into the neutral position. Then he kept the limb in flexion at the hip and knee by means of the double-inclined plane, which had been previously popularized and extensively used by Sir Astley Cooper up to the time that he discarded all methods of treatment except the pillow under the knee method. Sir Astley Cooper gave credit to White, of Manchester, England, as first suggesting the double-inclined plane method and added that it was later improved on by James, of Hoddesdon. The latter placed hinges at the angle of union of the inclined boards so that the height of the triangular plane could

be modified as desired. The double-inclined plane was a contrivance consisting of three boards placed in the form of a triangle, so that the base of this triangle would rest on the mattress and the thigh of the injured limb on the one side of the triangle, the knee over the apex and the leg over the other side. The principle of this method was that of Pott's semiflexion position of the limb, namely, to obtain muscular relaxation and the position of greatest comfort. A hinge connected the lower angle nearest the hip and another at the apex. The side over which the foot rested and the base formed a ratchet mechanism so that the altitude of the triangle could be varied according to the height desired. Pillows were placed over the apex and two sides of the triangle on which the limb was made to rest with comfort. The lower part of the leg was fixed by passing a cloth folded diagonally across its anterior part and making the ends fast to the sides of the bed, and a similar arrangement was adopted with the thigh.

The point of emphasis in Dupuytren's procedure was not so much in the method of fixation used as in the manner of reduction of the fracture. He flexed the thigh on the abdomen and the leg on the thigh and then gently "drew the thigh from abdomen." This was in contradistinction to the old accepted method of reduction by forceful application of extension and counterextension of the affected leg.

Belloq (1732-1807) devised a complicated machine (fig. 12) which secured extension by means of a jack. It consisted of two lateral splints connected below by a cross piece, on which worked a jack.

Boyer (1757-1833) obtained the same end (fig. 13) by adjusting a foot piece at right angles to his mechanical splint. He used a screw as a windlass to obtain permanent extension. His apparatus was similar to Desault's splint except that it was too complicated and expensive and was not practical for general use.

Brüninghausen, according to Boyer, was the first to place the limb in internal rotation in order to prevent external rotation. He fixed a stirrup to the foot of the bed, to which he tied both feet, using the sound leg to aid in extension. Then he bandaged a leather splint to the outer side of each leg, and the upper end of the bandage encircled the pelvis. He later gave up this form of treatment.

Henry Earle in his book published in 1823 described and illustrated his fracture bed. It was a complicated bed (fig. 14) mechanically adjustable to form a double-inclined plane. There were an opening in the bed for elimination of feces and urine and foot pieces to which the feet were fastened.

Velpeau utilized a method whereby a long roller bandage soaked in dextrin was applied around three wide pasteboard splints (anterior, lateral and posterior) from the toes of the injured limb up to the hip and around the pelvis in spica fashion. This is described in his book

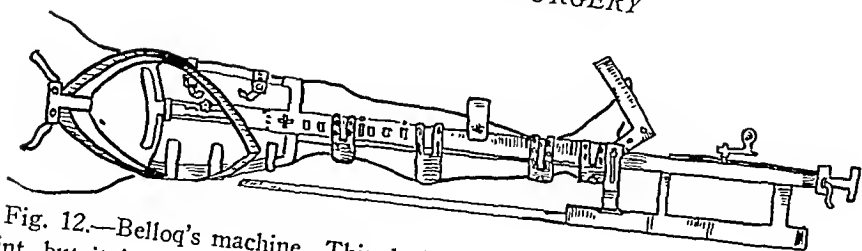


Fig. 12.—Belloq's machine. This device is also similar in principle to Desault's splint, but it is more complicated. A windlass device at the foot serves to exert traction. (From Belloq.)

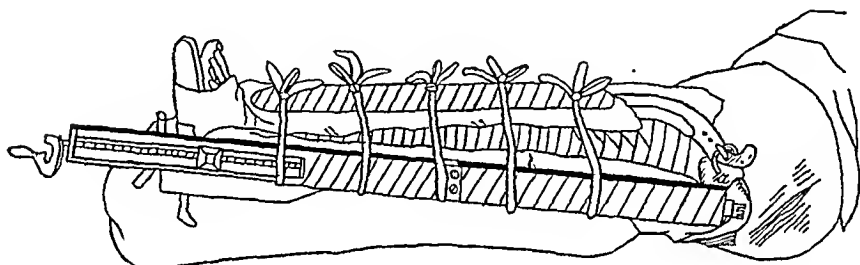


Fig. 13.—Boyer's splint. The principle is similar to that of Desault's splint except that a screw or jack device is used at the foot of the splint for traction purposes. (From Boyer.)

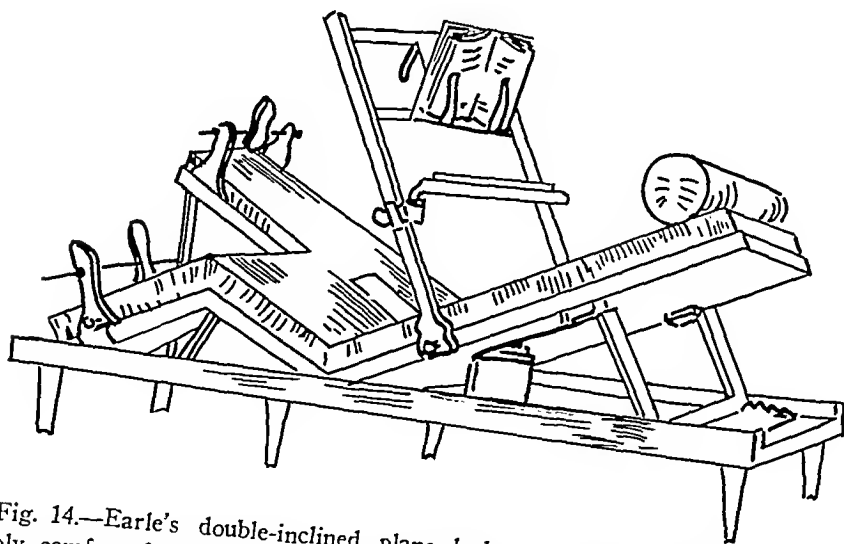


Fig. 14.—Earle's double-inclined plane bed. A complicated bed devised to supply comfort for the patient and immobilization of the fracture at the same time. The principle of the double-inclined plane which Sir Astley Cooper had popularized and the position of semiflexion advocated by Sir Percival Pott were employed here. The foot pieces to which the feet were strapped; the openings for elimination of excretions and for back rubs and the shelf for the dinner tray all were made to serve for convenience and efficiency. (From Earle.)

"Leçons orales" (1841). For extension he used the middle of a piece of strong bandage in the form of a figure of eight about the ankle and tied the ends to the foot post of the bed. A perineal band was applied to the groin and fastened to the head post for counterextension. When the bandages were thoroughly dried these two bandages for extension and counterextension were removed. Therefore, Velpeau was the first to use the hip spica bandage with a material, dextrin, simulating Whitman's plaster of paris spica bandage as the immobilizing agent.

Hamilton in 1860 described Gibson's modification of the Hagedorn splint. This splint consisted of a wooden footboard (fig. 15) to which both feet were fastened at right angles, and the lower ends of two crutches, which ends could be adjusted to the length of the limbs by means of pegs passed through one of the holes in each of the crutches. The crutches were well padded for comfort in the axillas. Thus this splint utilized the well leg for extension of the injured leg and the crutches for counterextension.



Fig. 15. Gibson's modification of the Hagedorn splint. Both feet are strapped to the footpiece so that the extended well leg acts as the agent of counterextension. The crutches are adjusted to their proper length and fixed to the footpiece. Hagedorn's original splint did not make use of the long crutches; the side splints reached up to about the level of the iliac crests and were bandaged to the legs and waist. (From Hamilton.)

Gurdon Buck, in 1861 introduced an improved extension apparatus (fig. 16) for fracture of the thigh. This method, known as Buck's extension, consisted of two long strips of adhesive tape about 2 inches (5 cm.) wide, applied to each side of the leg from the mid thigh to about 6 inches (15 cm.) beyond the sole of the foot. The ends of the strips were attached to a wooden block or spreader to relieve the pressure of the adhesive strips against the malleoli. The long strips were secured in place by crisscross and circular adhesive strips around the leg. A cord was attached to the center of the spreader and was made to pass over a pulley fastened to the end of the bed. A weight of 15 to 25 pounds (7 to 11 Kg.) was attached to the end of the cord for weight traction.

While all efforts up to this time were directed toward fixing the fracture by some form of splint or apparatus externally applied, no

attempts had been made toward open operation or internal fixation until von Langenbeck in 1858 first performed an open nail fixation operation on a fractured hip. The operation involved exposing the fracture site and nailing the fragments by means of a nail passing through the greater trochanter, the neck and the head of the femur. Aseptic surgery at this time was not yet heard of.

Koenig in 1875 and Trendelenburg in 1878 did the same type of operation as von Langenbeck's, but Lister in 1880 performed it with aseptic precautions.

Kocher in 1896 advised resection of the head of the femur for fresh fractures, because nonunion, in his opinion, was almost a foregone conclusion.

Returning to the splint methods of treatment of fractured hips, Nathan R. Smith in 1867 demonstrated the use of his anterior suspensory splint (fig. 17). He stated:

The anterior suspensory splint is applicable, with slight modifications, to all fractures of the femur. To none is it more appropriate, and in none has it accomplished more satisfactory results than in fractures of the cervix femoris, the events of which are so justly regarded as an opprobrium of surgery.

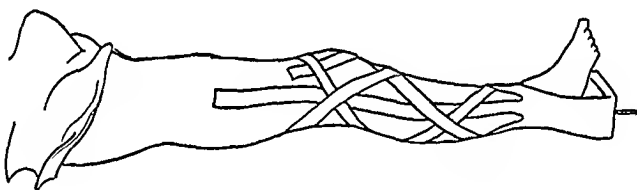


Fig. 16.—Buck's extension. (From Fowler.)

He claimed that his splint provided more comfort than the softest pillow and allowed the trunk more liberty in regard to position. For these reasons he advocated the use of this splint even though osseous union was not expected.

The splint was made up of a single rigid wire frame extending lengthwise from about the level of the iliac crest to the toes. The width corresponded approximately to that of the leg. The side pieces of this frame were strengthened by curved wire cross pieces at distances of about 5 inches (12.5 cm.). They had loops in their centers for attachment of hooks. The wire frame was bent into angles for the ankle and into slight flexion for the knee and for the hip. A muslin bandage was tightly wrapped around the wire frame and applied over the anterior aspect of the leg by means of bandages. To the hook above the knee and to the one at about the middle of the leg were attached the ends of a rope, about 5 feet (152 cm.) in length. The middle of this cord was made to pass through a loop at the end of a cord which was suspended from a system of pulleys fastened to the ceiling at a point perpendicular to a point at the middle of the leg. By slipping

the tenblock up or down the limb was elevated or depressed as desired. The foot of the bed was elevated by 2 inch (5 cm.) blocks. The weight of the body acted as counterextension. Extension was said to be accomplished by the obliquity of the cord, the variation of which would easily graduate the amount of extension desired. Smith claimed that extension was perfectly uniform and that the apparatus did not require the tightening or relaxation of bands from day to day.

Hugh Owen Thomas devised the Thomas ring splint in 1888. It consisted of an ovoid cast steel ring and a V-shaped cast steel rod, the two ends of which were fixed and attached to the ovoid ring. There was a slightly curved notch at the closed end of the V. The traction rope was tied here in cases of emergency traction treatment, for trans-

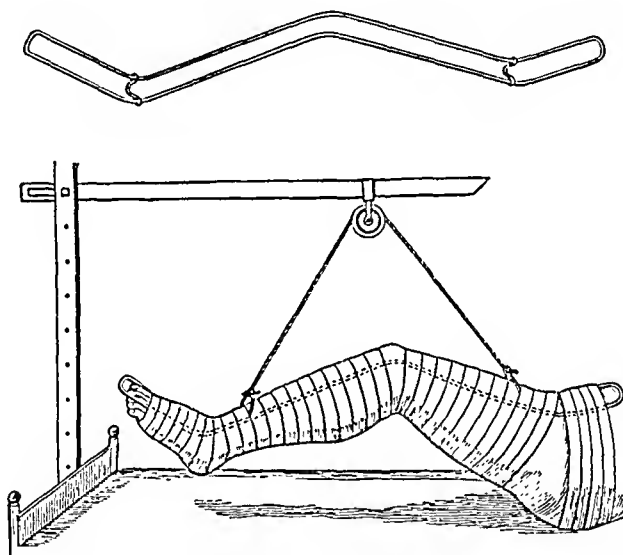


Fig. 17.—Anterior suspensory splint of Smith. (From Senn.)

portation. One arm of the V was shorter than the other, to allow for the obliquity of the groin from its external aspect inward. When in use the ovoid ring was padded with cotton or sheet wadding. The ring was passed around the leg in such a way that it was made to circumscribe the thigh at the groin, pressing against the tuber ischii. The leg was placed on towels which spanned the metal bars and were fastened to these by metal clips. Traction was applied by means of Buck's extension, previously described. This method later came to be used mostly in cases in which Whitman's plaster of paris spica was contraindicated.

Thomas himself preferred to use the Thomas-Ridlon splint (fig. 18), because it immobilized the hip joint above and below so that the hip corresponded to the center of the appliance (lengthwise).

Senn, around 1889, used a plaster of paris spica bandage (fig. 19) with a screw device over the lateral aspect of the greater trochanter, exerting graduated lateral pressure to force the two fragments together.

At about the same time, 1889, Ridlon popularized the Thomas-Ridlon single hip splint. This was devised to maintain fixation of the fragments and to allow the patient to be ambulatory by means of crutches. The splint consisted of a main stem, a chest band, a thigh band and a calf band. The main stem was placed along the posterior aspect of the limb and buttock of the affected side and up the back to

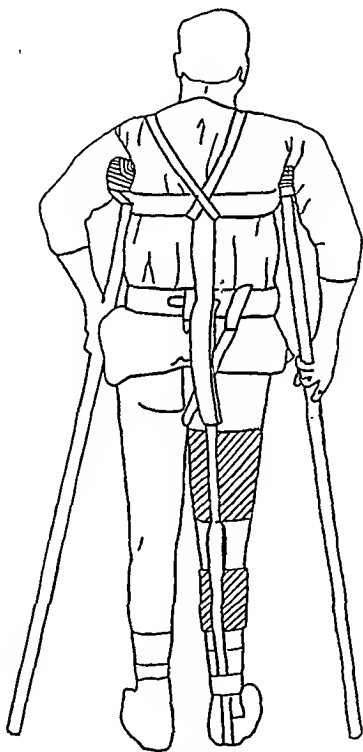


Fig. 18.—Thomas-Ridlon splint for immobilization of the hip joint. (From Keen.)

the level of the axilla. It was curved over the buttock to conform to the contour of the part.

To the lower end, just above the ankle, was fastened (by one rivet) the calf band. The thigh band was also riveted to the stem at about the level of the great trochanter. The chest band was fastened at the upper end of the stem at a level just below the axillas. All these bands were open anteriorly. A hole was forged in each end of the chest band so that the shoulder straps might be attached to it and crisscrossed over the shoulders, to be fastened to the attachment of the chest band to the stem.

The splint was bent to fit the patient approximately, and was padded on the side next to the skin.

Scudder advised the use of Senn's lateral pressure pad over the great trochanter along with the Thomas-Ridlon splint. The limb was bandaged to the splint if retentive traction was not necessary. If the latter was called for, the shoulder straps were omitted.

In 1891, C. R. Ruth first used the "anatomic method," the combined longitudinal and lateral traction method that was introduced by Maxwell in 1871. The method became popularly known as the Maxwell-Ruth method (fig. 20). Maxwell claimed no originality for this mode of treatment but gave due credit for the discovery to G. W. Phillips (fig. 21) who introduced it in 1869. The lateral traction was arranged in such a way as also to maintain internal rotation of the hip,

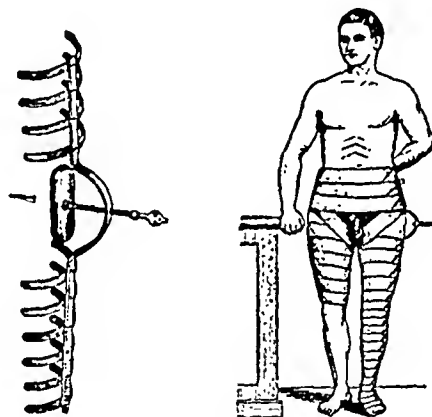


Fig. 19.—Senn's plaster of paris spica bandage, with a screw device over the lateral aspect of the great trochanter. (From Senn.)

i. e., by means of a wide strip of adhesive plaster, application of which was started at the outer aspect of the upper third of the thigh, proceeding internally over the anterior surface of the thigh and then over the posterior aspect to beyond the outer aspect of the thigh. A rope was attached to this end of the adhesive tape and was made to go over a pulley fixed at the side of the bed. Longitudinal traction was obtained in the usual manner, i. e., by Buck's extension.

It is stated in Wilson and Cochrane's book that "the resultant of the two forces acting at right angles to each other is represented by a line passing between the two and corresponds more or less closely to the normal axis of the neck of the femur." Reduction by the Maxwell-Ruth method consisted of flexing the thigh at a right angle to the trunk. Then an assistant exerted an outward pull in the axis of the upper end of the lower fragments. Traction on the limb was made in the long axis of the body.

WHITMAN'S METHOD

With the opening of the twentieth century a great milestone loomed in the evolutionary progress of the treatment of fractures of the hip. Royal Whitman, of New York, gallantly revived an almost dying

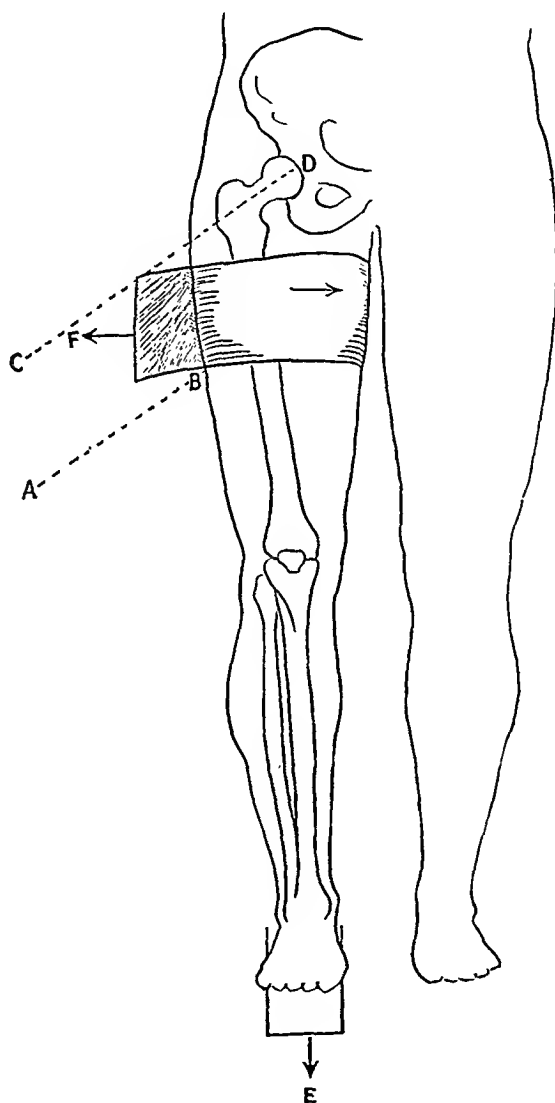


Fig. 20.—Maxwell-Ruth method of combined lateral and longitudinal traction. (From Wilson and Cochrane.)

interest in patients with such fractures and rekindled anew the flame that Ambroise Paré and Sir Astley Cooper had so enthusiastically borne in their trail-blazing efforts. In 1904 Whitman introduced the plaster of paris hip spica-abduction method of fixation, which was

to become for a time the accepted treatment all over the world. Bick, in his book on the History of Orthopedic Surgery, 1930, stated:

Whitman's method has become a boon to the thousands of aged individuals, who, when treated by previous supportive measures had only the prospect of spending their few remaining years bedridden or in a wheelchair. He has succeeded in effecting rehabilitation of many of these cases, and among the more aged ones, has restored to a comparatively adequate function a limb which otherwise would have been entirely incapacitating.

In an article entitled the "Abduction Treatment of Fracture of the Neck of the Femur," appearing in *The Journal of the American Medical Association* of Dec. 3, 1921, Whitman stated: "The object of treatment of a fracture is to restore the symmetry of the broken bone, because the primary cause of nonunion is separation of the fragments and because deformity entails loss of function."

"The traction treatment is justified," he continued, "for fractures of the shaft of the femur but not of the neck of the femur. In the latter case the neck projects laterally and traction can at best appose the fragments in an insecure relation."

He stated further:

In a recent treatise on fractures it is stated that the first indication is to save life, second to get union, third to correct or diminish displacements. This in fracture of the neck of the femur actually represents the subordination of surgical principles to inadequate mechanics. The abduction treatment is by contrast radical and revolutionary, because, being mechanically adequate for its purpose, fracture of the neck of the femur, in all operable cases, is treated like other fractures, in complete disregard of the qualifications and restrictions of conventional practice and of the conclusions that uphold it.

The abduction treatment is adequate because it utilizes the anatomy of the hip joint both to correct deformity and to appose displaced fragments, external appliances being entirely subsidiary to the internal, or natural splint.

The Whitman method of treatment consists in reducing the fracture by direct traction of the leg longitudinally with the patient under anesthesia and abducting the injured limb, while traction is being applied, to the normal 45 degrees position and internally rotating the limb. This is done on a special fracture table, the Hawley table, with the pelvis supported on a pelvic rest. Two assistants then maintain both limbs in about 45 degrees of abduction. A plaster of paris spica bandage from the toes of the affected limb to the chest is applied over stockinet and a layer of sheet-wadding. Scudder, in his book, advised flexing the thigh according to Maxwell (in addition to Whitman's method of reduction) in order more readily to reduce the fragments. He considered Whitman's abduction method of treatment sound and declared that it was here to stay.

Cotton, shortly afterward, introduced the impaction method of treatment. In his book on fractures and dislocations, published in 1910, he stated (page 477, footnote):

I believe the time is coming when it may seem wise, in these cases, perhaps in all unimpacted fractures of either neck or base of neck that are fit to etherize, to produce impaction by driving home the trochanter (protected by felt, of course) with a heavy mallet. I have done this in one case with admirable results.

Fred H. Albee, in 1912, introduced to this country the autogenous bone graft in the treatment of these fractures. Before describing this method, it may be better to take up again the early history of the employment of open operation. As has been noted, von Langenbeck, in 1858, was the first to attempt an operation, using a nail as the fixative agent. Then followed Koenig, in 1875, Trendelenburg, in 1878, and Lister, in 1880, all of whom used the nail (fig. 23). Trendelenburg and Koenig also advised suture of the bone with wire. Kocher in 1896 advised resection of the head of the femur. In 1897

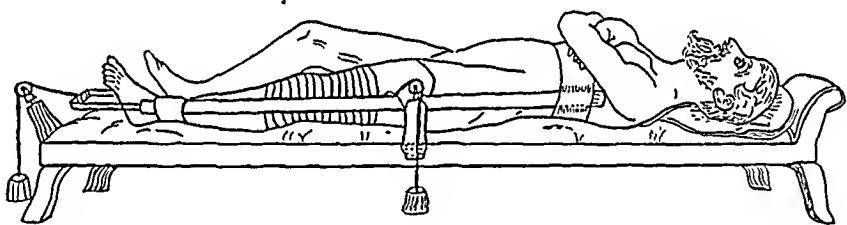


Fig. 21.—Longitudinal and lateral traction apparatus. This device includes a long wooden side splint, Buck's extension for longitudinal traction and a thick broad cloth band around the upper part of the thigh for lateral traction by means of a weighted cord attached to the band passing over a pulley. (From Phillips.)

Julius Nicolaysen reported on 13 cases of fresh fracture treated by means of a steel spike. He stated that when treated by this method the patient was immediately able to take up more comfortable positions. His technic consisted of applying manual traction on the affected limb and driving a steel spike 15 cm. long 5 cm. below the upper edge of the trochanter, so that the head of the spike remained outside the skin. A fenestrated plaster of paris spica was applied and maintained for eight to ten weeks. He did not allow weight bearing for ten or twelve weeks.

Pierre Delbet was the first to use the metal screw (fig. 24). He introduced this method in 1907. Dujarier and Delbet made extensive use of it. A heavy wormed metal screw 7, 8 or 9 cm. long and 6 cm. thick was employed. The screw was only partly wormed, so that an intimate opposition could be established. The screw was inserted about 1.5 cm. below the crista trochanterica. He placed 15 to 20

pounds (6.8 to 9.1 Kg.) of weight traction on both feet for a few days. Later he applied a walking splint for about four weeks.

While up to this time physicians performing internal fixation utilized metal as the fixative agent, F. Faltin stated that Hahn in 1909 was the first to use the bone peg from a tibial graft instead of the metal spike or screw. Borelius in 1911, reported a case of pegging.



Fig. 22.—Whitman's method. Abduction in a plaster of paris hip spica bandage. (From Whitman.)

Fred H. Albee, of New York, employed the autogenous bone peg as the fixative agent for the first time, in 1912. Albee stated that the surgeon has the following obstacles to contend with in cases of this fracture, namely: (1) the mechanical disadvantage of not having

end to end stress as with other fractures; (2) deficient osteogenesis due to the presence of little or no periosteum and to a poor blood supply; (3) the intracapsular nature of the fracture and the possible detrimental effects of the synovial fluid present; (4) the interposition of soft parts, and (5) the relatively small diameter of the neck of the femur.

He therefore offered the autogenous bone peg as his method of treatment to overcome these obstacles. He stated:

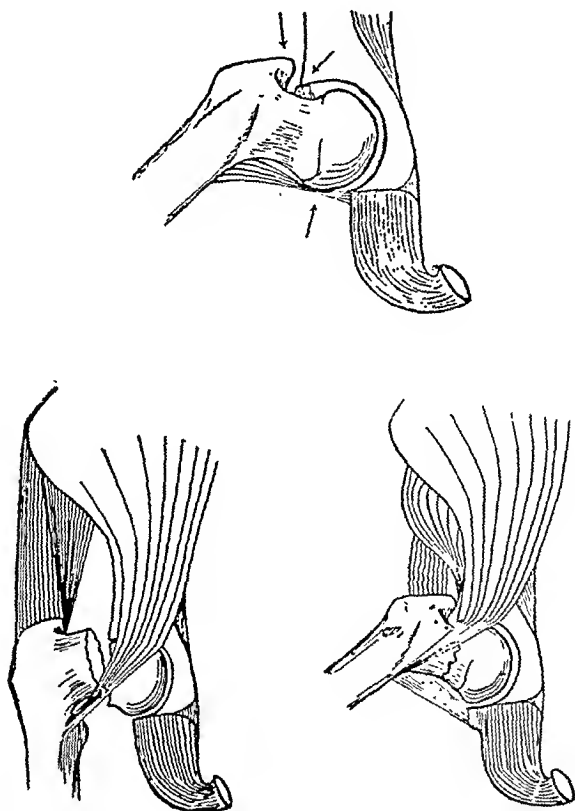


Fig. 22a.—Original diagrams from Whitman (1902).

A strong autogenous bone peg accurately fitted into a hole drilled longitudinally through the neck of the femur, with the fragments in good position, offers unquestionably, the most ideal condition for the rapid and satisfactory union, in good position, of this difficult fracture.

The following is the technic he uses (fig. 25):

1. The patient is placed on the Albee table.
2. A curved incision is made, beginning a fingerbreadth inside of the anterior superior spine and curved downward 3 to 5 inches (7 to 12.5 cm.) along the inner border of the sartorius.

3. The muscles are retracted; the point of fracture is exposed, and the interposed soft tissue, if any, is cleared from between the fractured ends, which are curetted and (if the fracture is old) freshened.

4. The limb is placed in abduction and traction.

5. A lateral incision is made over and below the greater trochanter, which is exposed.

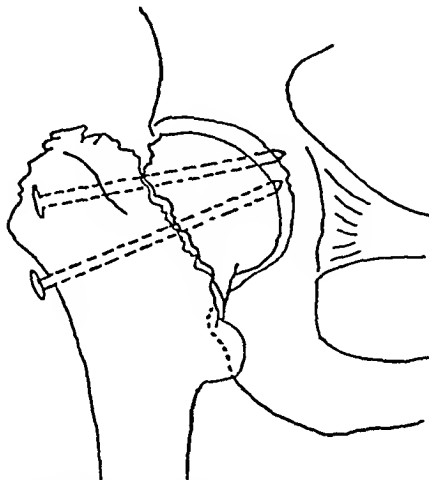


Fig. 23.—Two plain twelvepenny nails such as were formerly used in open operation for nailing the fragments together. (From Speed.)

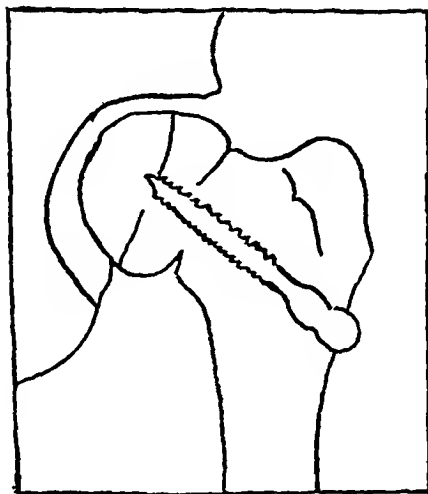


Fig. 24.—Delbet screw. (From Bassett.)

6. With a motor drill a hole $\frac{3}{8}$ inch (0.9 cm.) in diameter is made.

7. A tibial graft which has been shaped into a peg by a dowel shaper is inserted into the drill hole and driven home.

8. The wounds are closed.

9. The limb is placed in the Whitman abduction plaster of paris spica extending from the toes to the midthoracic region.

10. Windows are cut in the plaster three weeks after the operation, and the wounds are dressed.

11. The long plaster spica bandage is kept on for six weeks and a short one for six additional weeks.

A graft from the fibula instead of the tibia was used as the bone peg for the first time by Delbet in 1911.

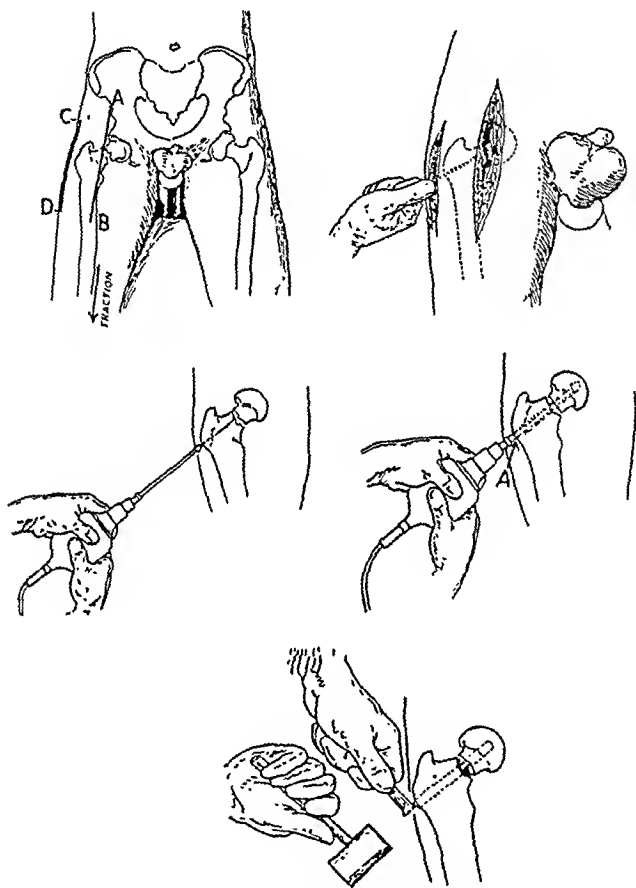


Fig. 25.—Use of the autogenous bone peg as the fixative agent. (From Albee.)
AB and CD represent cutaneous incisions.

Ellis Jones in 1932 reported his experience with trochanteric transplantation of autogenous bone (fig. 26).

The advantages of the fibular bone graft over the tibial peg as claimed by Davison are:

1. It is the size of the bone adapted to the purpose.
2. The requisite length is easily obtainable.
3. It is irregularly round and will not rotate like a dowelled peg.

4. It is a tube of compact bone which is mechanically stronger than the same amount of compact bone in a solid piece.
5. It presents a continuous circular surface of the cambrium layer to the host bone for grafting and to simulate osteogenesis in and around the defect.

The operation is briefly described as follows:

With the patient on the Hawley table, an anterior incision, beginning a little below the anterior superior iliac spine and extending downward, is made, and the site of fracture is exposed. A second incision is made along the outer aspect of the thigh, exposing the greater trochanter. At an angle of about 45 degrees with the shaft of the femur an opening is made through the cortex with a gouge or electric drill. A canal is made, slightly smaller than the size of the fibular graft (a segment of the lower part of the fibula), and the graft is then driven home. A plaster of paris hip spica bandage is applied from the toes of the affected side to the axilla, including the opposite thigh. This is kept on for eight weeks, with the affected limb in extreme abduction, extreme external rotation and slight flexion at the thigh. Immobilization is maintained for eight weeks.

In the book "Autoplastic Bone Surgery" by Davison and Smith, published in 1916, there is a description of 3 cases in which this method was used. Mayo, Nordenbos and Kelvington have also used this method to a considerable extent.

E. H. Bradford in 1919 presented a method of ambulatory treatment by application of an abduction traction splint.

R. Hamilton Russell, of Melbourne, Australia, in 1924, reported a method of skin traction which he had been using for several years in such cases. It consisted of adhesive plaster (fig. 27) applied to the leg of the affected side as for Buck's extension, a sling made of toweling or felt in which the knee was placed and a system of pulleys so placed as to obtain a slight amount of flexion at the knee and yet effect traction. This is known as the Russell Traction.

O. P. D. Wilkie, of Edinburgh, Scotland, in 1927, described a method of abduction and immobilization of both legs by means of plaster bandages (fig. 28) to the latter. Again, the utilization of the principle of well leg extension was applied in a new method. Flexible copper cuffs were incorporated in plaster boots to each leg, with the sound leg in internal rotation and both legs in 45 degrees. Then a brass abduction rod was attached to the jointed attachments on the copper cuffs. Later a window was cut in the plaster of the sound limb so that the latter might be taken out and exercised from time to time.

METHOD OF SMITH-PETERSEN

An epoch-making era was ushered in, in 1925, when Smith-Petersen, of Boston, introduced his monumental contribution in this field. This consisted of an ingenious three-flanged nail which he used

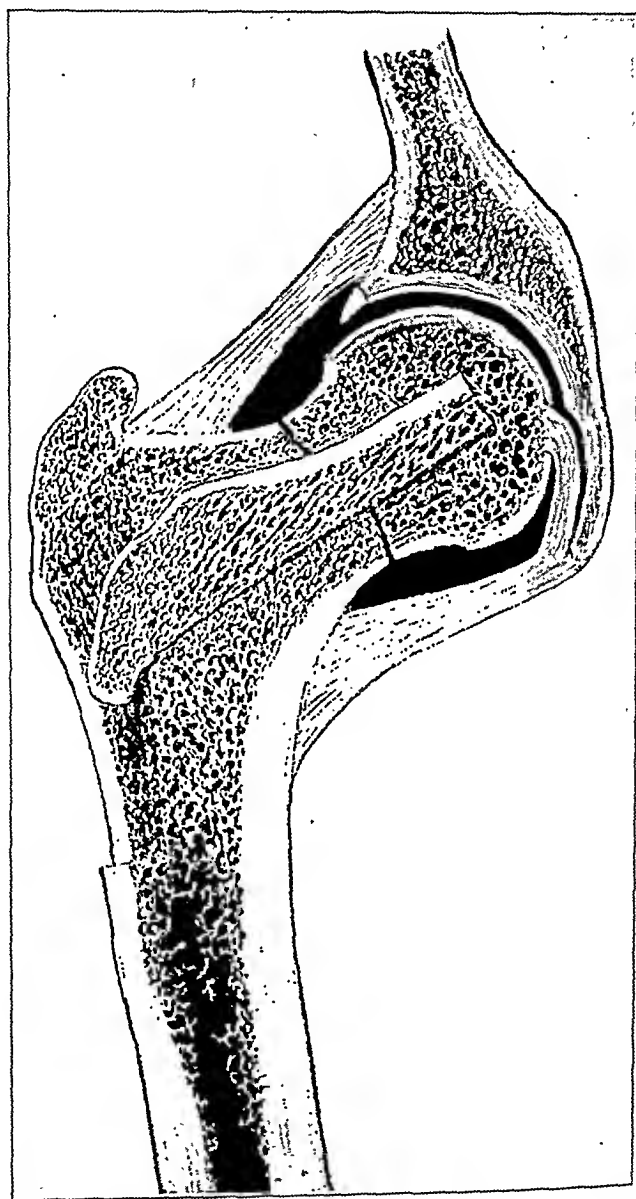


Fig. 26.—Trochanteric transplantation of autogenous bone. (From Ellis Jones.)

for transfixation of such fractures. While in the past two or three decades the Whitman plaster spica method had held sway as the method of choice, this new flanged nail pegging of the fractures has gained wide and rapid popularity.

The important feature of this operation lies in the shape of the nail. Its three flat blades are arranged cart wheel fashion and when inserted grip the bone firmly so that the bone cannot rotate about the nails on its axis. This renders fixation and approximation of the fragments more satisfactory. No postoperative agent of external fixation

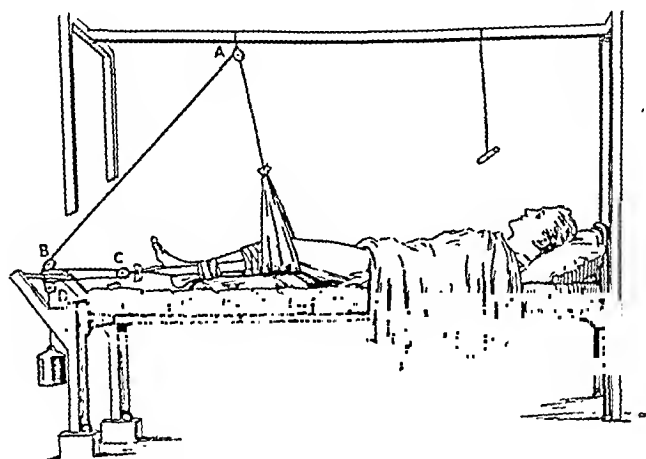


Fig. 27.—Traction with the knee in slight flexion. (From Russell.)

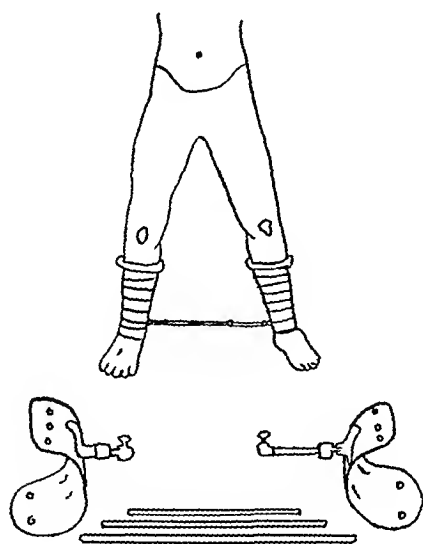


Fig. 28.—Abduction and immobilization of both legs. (From Wilkie.)

is necessary, because of the strength and security provided by the metal (stainless steel) nail. Early activity is allowed, convalescence is rendered more comfortable and is greatly shortened.

In November, 1931, Smith-Petersen, Cave and Van Gorder reported their description (figs. 29 and 30) of this operation. He made a curved incision along the crest of the ilium down the anterior

border of the tensor fasciae femoris, curving posteriorly across the insertion of this muscle into the iliotibial band in the subtrochanteric region. Then a musculoperiosteal flap was reflected from the dorsal aspect of the ilium, and the capsule of the hip joint was exposed. The fracture was reduced (after incision of the capsule) by internal rotation, extension and abduction of the limb. A point on the lateral aspect of the greater trochanter just below the attachment of the gluteus medius and the gluteus minimus muscles was located. About 1 inch (2.5 cm.) below this point, a starter the shape of the three-flanged nail, although heavier and stronger, was inserted with a mallet until the cortex was traversed. The starter was removed and the

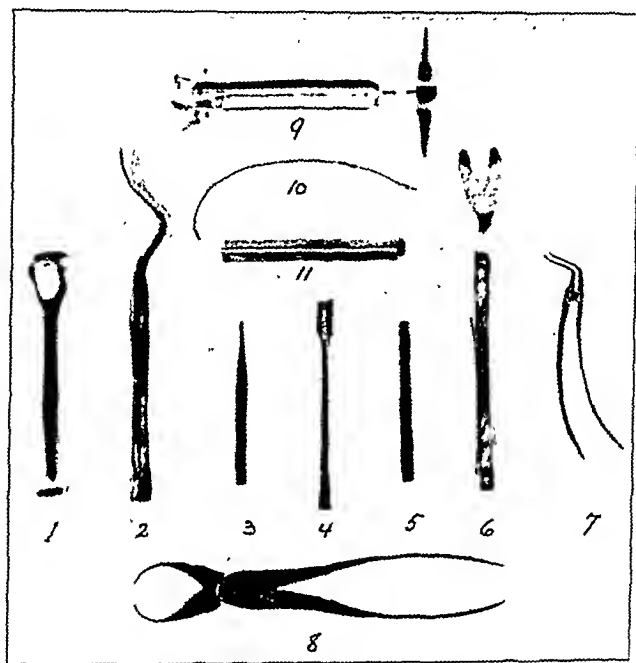


Fig. 29.—Instruments used for Smith-Petersen's operation: (1) impactor, (2) spatula, (3) nail-set, (4) starter, (5) nail-set, (6) spatula, (7) distractor, (8) obstetric forceps, (9) nail extractor, (10) flexible steel measure, and (11) three-flanged nail. (From Smith-Petersen, Cave and Vangorder.)

nail was introduced and tapped with a mallet until the head of the bone was pierced. At this point, the impactor, an instrument which impacts the two fragments by means of blows from a mallet, was used. (This instrument also assists in the progress of the nail into the head fragment.) The wound was closed in layers.

The postoperative management consisted of traction of 5 pounds (2.3 Kg.) for about three or four weeks. At the end of this time a bivalved short plaster spica in 10 or 15 degrees of abduction was used for walking only. [NOTE.—No external fixative agent is used at present.]

Weight bearing was allowed three to five weeks after the operation. Support in a plaster or jointed leather spica was used for from three to six months.

The results obtained in 20 cases reported by the author of this method showed osseous union in 15 cases, or 75 per cent; nonunion in 3 cases, or 15 per cent, and death from sepsis in 2, or 10 per cent.

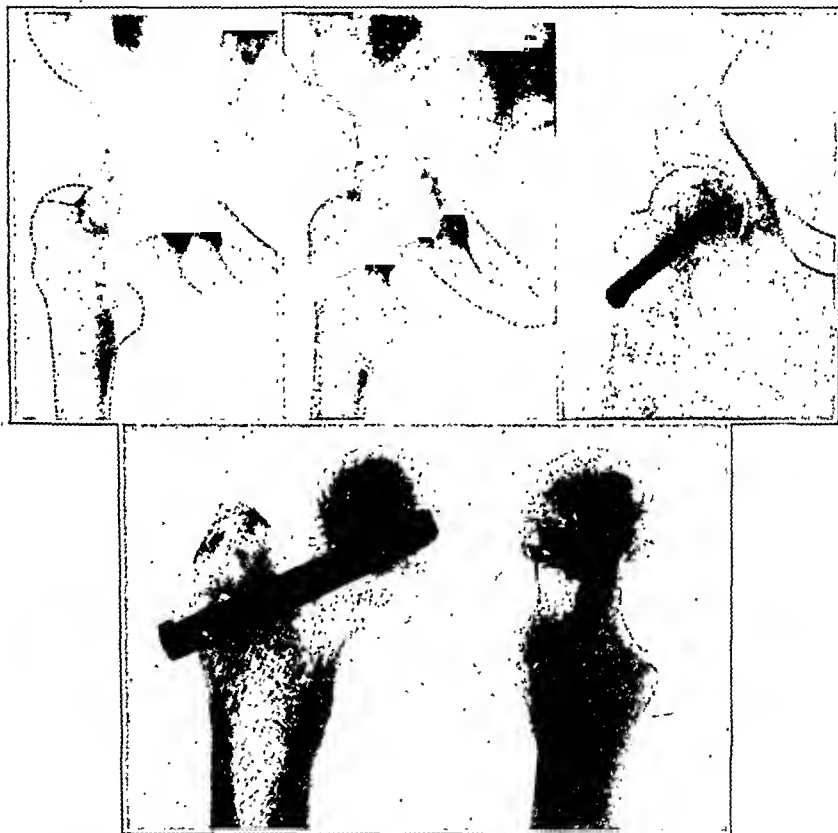


Fig. 30.—Preoperative roentgenograms and roentgenograms taken four and six weeks after operation. (From Smith-Petersen, Cave and Vangorder.)

He concluded that in the treatment of joint fractures, anatomic reduction and early function are the two outstanding principles.

In a later paper on this subject, which Smith-Petersen presented in October 1936, he described several modifications that he had employed in his more recent cases. Instead of the "open" method of operation which he used at first, whereby the hip joint was fully exposed, a formidable procedure to be sure, he had taken up the Wescott "blind-nailing" extra-articular method, which will be described later. He also had substituted the Wescott modification of the Smith-Petersen

nail, made of one piece of metal, for the type of nail previously used, which was made up of a headpiece welded on the shaft. The Leadbetter method of reduction, i. e., of flexion of the thigh, traction in the axis of the thigh and internal rotation, extension and abduction of the leg, had replaced the Whitman method, which he formerly employed.

Up to the time of publication of the second paper he had treated only 20 fractures by this new method and felt that the number of

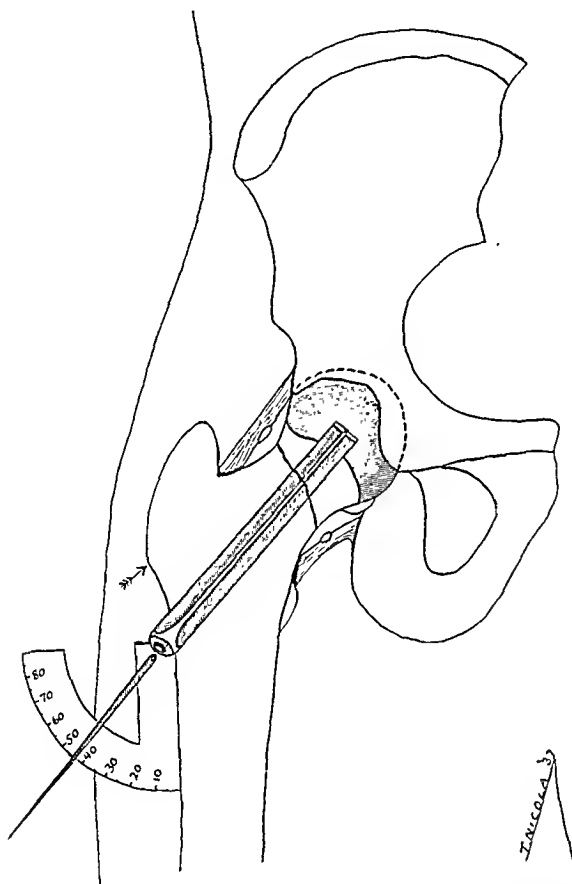


Fig. 31.—Technic of the Smith-Petersen operation. A nail is inserted 1 inch (2.5 cm.) below the base of the greater trochanter, as indicated by the arrow, at an angle of about 45 degrees, as shown by the protractor. Note the Wescott type of solid metal nail used instead of the former two-piece nail of Smith-Petersen.

cases as well as the time of observation was not sufficient to enable him to give a correct analysis of end results obtained by this method.

Sven Johansson, of Göteborg, Sweden, in 1932 used the same method as Smith-Petersen except that he used the "blind-nailing" type of operation (fig. 32). Instead of an extensive open operation

necessitating opening of the hip joint, Johansson inserted the nail "blindly" through a small lateral longitudinal incision over the greater trochanter; utilizing a Kirschner wire already inserted into the head and neck, he threaded the wire through a central canal in the nail as a guide.

Jerusalem, of Vienna, Austria, employed Johansson's method, using a nail with a hole bored through the head instead of a canalized one.

Wescott, of Roanoke, Va., in July 1932, reported a method (fig. 33) whereby he inserts the Smith-Petersen nail by the "blind" or extra-articular method. First he determines the angle of anteversion of the forward angle of the neck of the femur with the shaft by means of a roentgenogram. Then the length of the nail to be used is calculated by taking a roentgenogram of the normal hip with the leg in about 20 degrees internal rotation and a measuring rod strapped with adhesive tape to the trochanter. From the film the length of the neck is compared with the marks on the measuring rod, and thus the length of the nail is estimated. Also the angle of the nail with the shaft is determined.

Next the patient is anesthetized, and the fracture is reduced by flexing the thigh and exerting traction in the line of the thigh. Internal rotation is then performed. Abduction is not necessary, according to Wescott, because of danger of producing a valgus deformity. The assistant maintains the leg in internal rotation. Roentgenograms are taken to determine proper reduction.

A lateral incision of $2\frac{1}{2}$ to 3 inches (6.2 to 7.5 cm.) is made over and below the greater trochanter. One-half inch (1.2 cm.) below the "vasternus line" narrow slits are made with an osteotome to receive the blades of the nail. The protractor is placed on the shaft of the femur with the lever placed on the angle already figured out. The nail is inserted and driven into the neck. The fracture is then impacted with an impactor. The wound is closed. Roentgenograms may be taken if it is desired to follow the course of the nail.

The patient is allowed in a wheel chair in from twenty-four to forty-eight hours and on crutches after a few days.

The nail fixation method has been also adopted by King, of Australia. He follows the Johansson method. The new Hawley table with the shock-proof fluoroscope and x-ray attachments is used as an aid in following the progress of the nail.

O'Meara, of Worcester, Mass., has used Wescott's method since 1933.

Roger Anderson, of Seattle, in 1932, revived the method (fig. 34 and 35) of utilization of well leg extension. The Brünighausen, Gibson, and Hagedorn splints, and the Wilkie apparatus as previously described, employed the same principle of well leg extension, with the

exception that Anderson used skeletal traction on the injured limb, which traction was not used in the others. Brüninghausen also was among the first, if not the first, to obtain counterextension by means of well leg extension. In fact, Anderson stated in his article "that ancient history records the army mode of handling broken legs by pulling the injured leg to its normal length and bandaging it to the

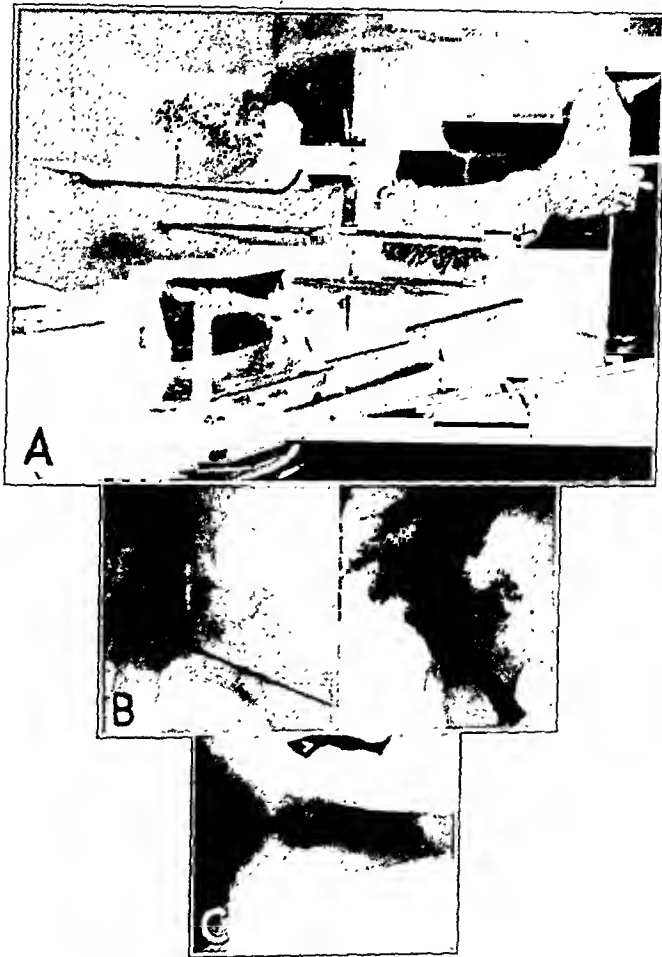


Fig. 32.—*A*, insertion of a Kirschner guide wire, followed by insertion of the Smith-Petersen nail; *B*, apparatus for accurate insertion of the Kirschner wire. (From Johansson.)

opposite or well leg in attempt to keep reduction and immobilization." He stated that C. K. Coonse and Carl P. Jones have also used the sound leg for both immobilization and countertraction.

The principle of Anderson's method is as follows:

If reduction of the fracture is made by traction in a parallel position to the sound leg and the well leg is maintained in a counter-extension, the x-ray shows

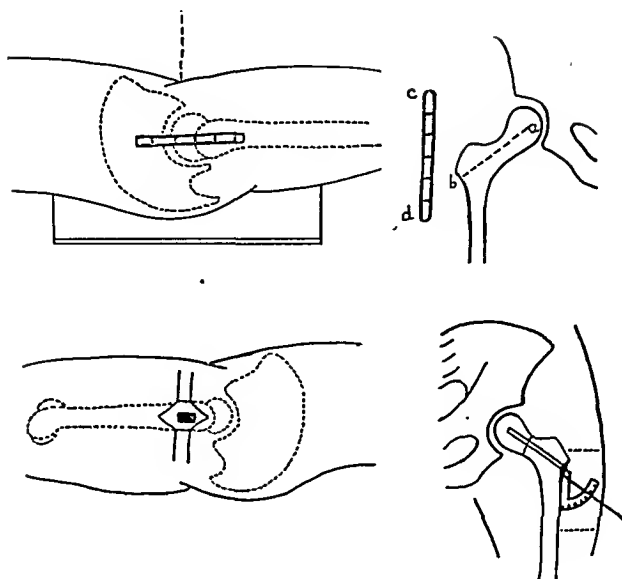


Fig. 33.—“Blind” or extra-articular insertion of the Smith-Petersen nail. (From Wescott.)

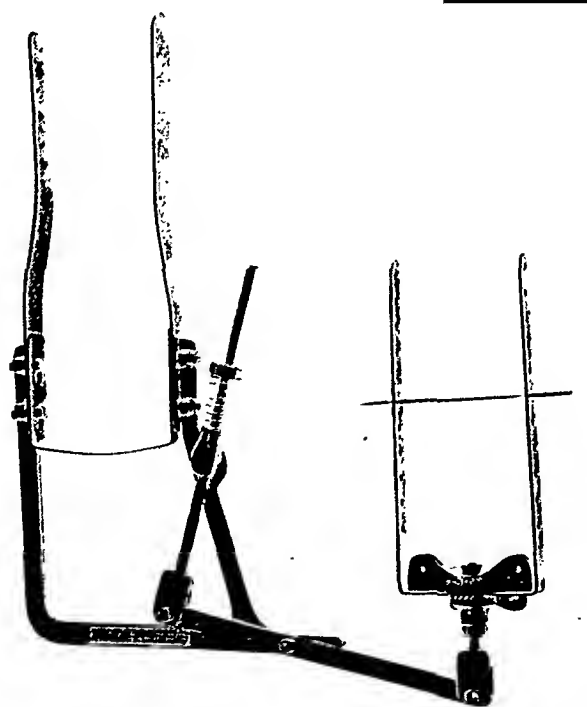


Fig. 34.—Splint providing skeletal traction on the injured limb. (From Anderson.)

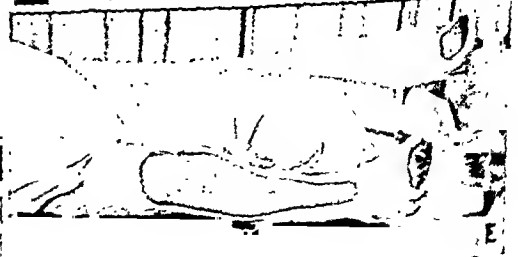
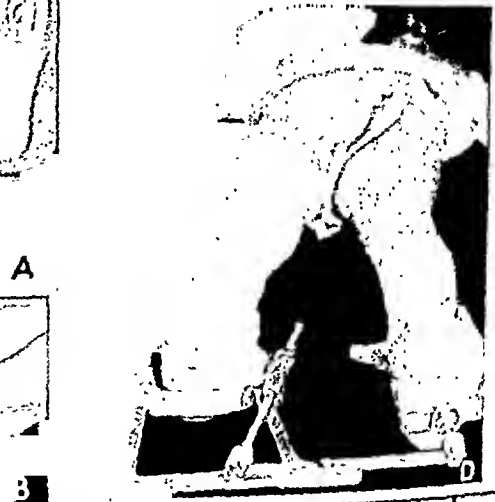
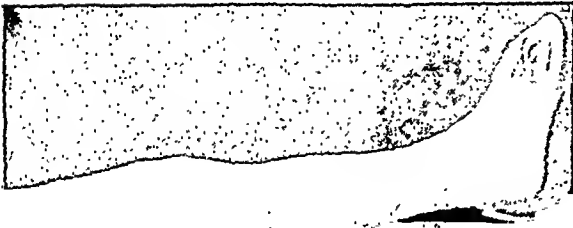
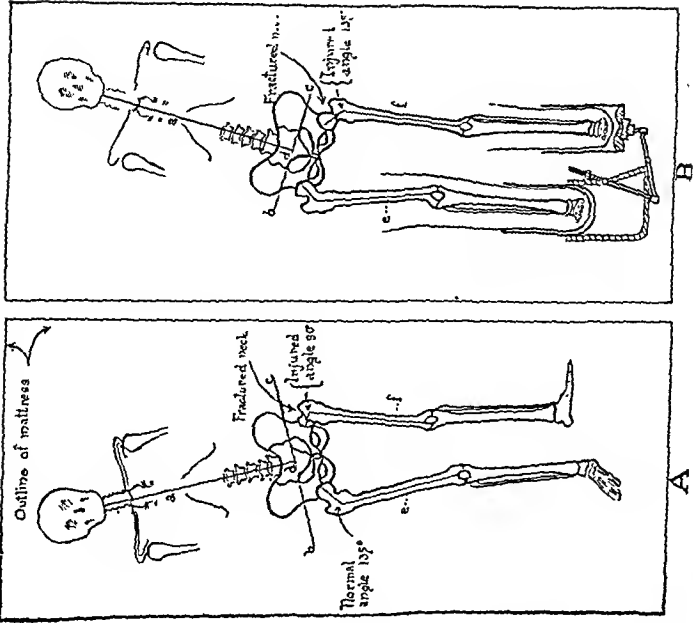


Fig. 35.—Treatment by skeletal traction. (From Anderson.)

that the traction forces the acetabulum down on the injured side, while counter-traction forces the well acetabulum up, thereby changing the angle of the transpelvic line with the axis of the injured leg, from an acute to an obtuse angle. This in turn forces the angle of the neck with the shaft of the injured femur into the normal position of 135 degrees.

The apparatus consists of a counter-traction portion and a traction portion. The former consists of a frame to which is attached a thin flexible counter-traction stirrup, with removable base to be molded later to the cast of the well leg.

A transverse lever which connects this counter-traction side to the traction part is pivoted to this frame, the axis of which is about six inches distal to the sole of the well foot. On a threaded traction rod which is joined to this end of the lever is a nut to furnish traction force, and a coiled spring to ensure a smooth, flexible, yet constant traction.

The traction portion of the splint is made up of a stirrup, with perforated sides for the insertion of the pin, and is connected to the lower arm by the traction rod, through the center of which at its proximal end is the rotation adjustment with its lock nut for internal and external stability.

The cause of nonunion of such fractures has been variously stated, interference with the circulation and improper immobilization having been prominently mentioned. It has been stated that with fractures of the neck of the femur ("intracapsular") the blood supply to the head portion is cut off because of the interruption of the nutrient artery from the distal portion of the neck and the capsular and periosteal arteries; also that arteriosclerosis causes an occlusion of the artery that courses through the ligamentum teres; this is a common observation post mortem. Therefore, Bozsán in 1932 attempted to remedy this situation by drilling holes through the trochanter and neck into the head fragment to establish circulation and promote osseous union. He reported 2 cases in which this method was used with good results.

The position of the leg both in the reduction of the fracture and in the maintenance of immobilization has long been the subject of considerable interest and attention. Hippocrates preferred to have fractures of the femur in extension; Rhazes (850-932), on the other hand, of all the ancients was the only one to recommend the thigh to be laid "in a somewhat bent position." While it is not known whether the ancients were aware of the existence of fractures of the neck of the femur, still this shows that authorities differed in opinion as to the position of the limb in the presence of fractures of the leg, and this trend has continued up to the present day. Desault, Boyer, Hagedorn, Thomas, Ridlon, Liston and Whitman emphasized straight leg traction employed for either reduction or immobilization for fractures of the neck of the femur; Pott, Dupuytren, Cooper, Earle, Hodgen, N. R. Smith, Maxwell, Ruth, Russell, Leadbetter and Gaenslen, on the other hand, preferred a position varying from semiflexion to flexion of the hip and knee, with or without traction.

Leadbetter in 1933 devised a method of reduction of this fracture, which is known as the "Leadbetter method." Manipulation consists of flexion at the hip at 90 degrees with the thigh flexed at the knees at 90 degrees with the lower part of the leg. Manual traction is exerted in the axis of the flexed thigh, with slight abduction of the femoral shaft. The leg is then slowly circumducted into abduction, internal rotation and extension. The heel is allowed to rest in the palm of the examiner's hand to see if eversion of the foot takes place. If the neutral position of the foot is maintained with this test, reduction is then considered successful; this is known as the "heel-palm test." Then the limb is placed in a plaster of paris body spica bandage, with little padding. This method of reduction is becoming very popular.

Laurence Jones, of Kansas City, Mo., devised a closed double screw method for reduction and fixation of the fracture (fig. 36). He

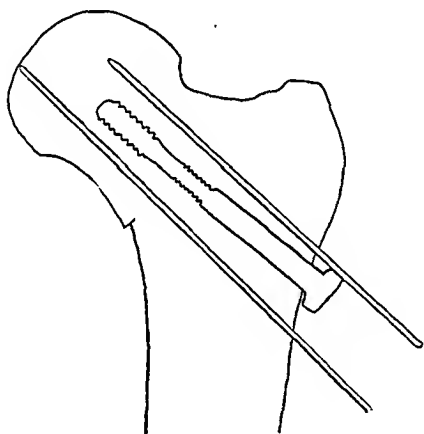


Fig. 36.—Closed double screw method for reduction and fixation of the fracture. (From Laurence Jones.)

reported this method in the *Annals of Surgery* in February 1933. The double screw consists of a proximal portion, a burr, a shaft with a square end for a socket wrench, and a traction cap with a groove for a screwdriver.

The procedure is as follows:

1. Measurement and localization of the fragments are done by means of roentgen examination.

2. Two Kirschner wires are inserted through the neck and head of the greater trochanter as guides and to keep the head fragment from rotating.

3. Plaster boots extending from the toes to 6 inches (15 cm.) above the knee are made preoperatively to prevent turning at the ankle; extension straps are placed over these, and the legs are maintained in the Whitman position.

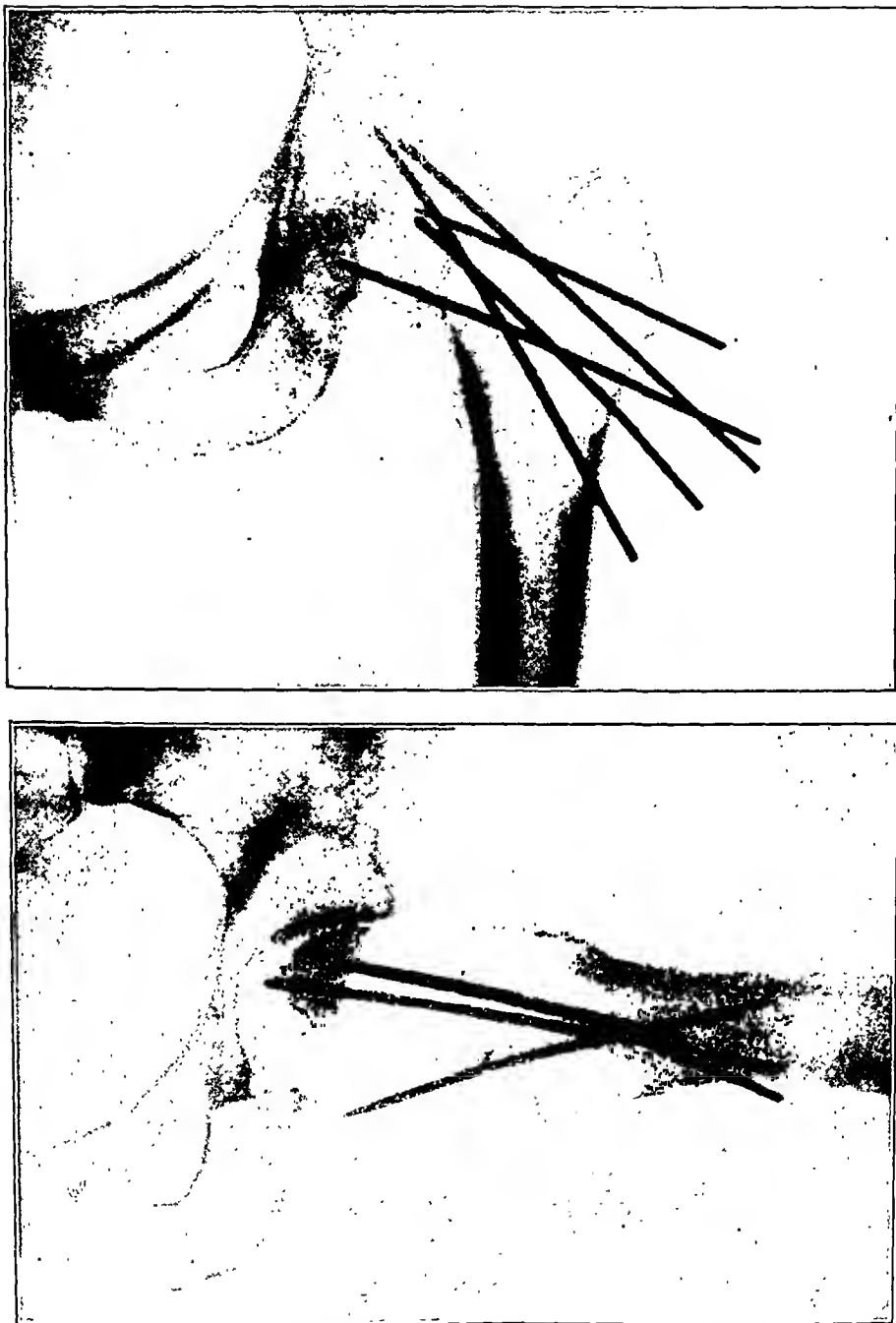


Fig. 37.—Insertion of rustless steel fixation spikes into the fragments. (From Gaenslen.)

4. Local or general anesthesia is employed.
5. A 2 inch trochanteric incision is made.
6. Kirschner wires are inserted.
7. Anteroposterior and lateral roentgenograms are taken to determine the position of the wires.
8. A drill hole is made between the wires, and the proximal portion of the screw is inserted with a socket wrench.
9. The distal or traction cap of the screw is threaded on the shaft of the proximal part and tightened with a screwdriver. The fragments are impacted with an impactor. A few more turns with the screwdriver are taken.

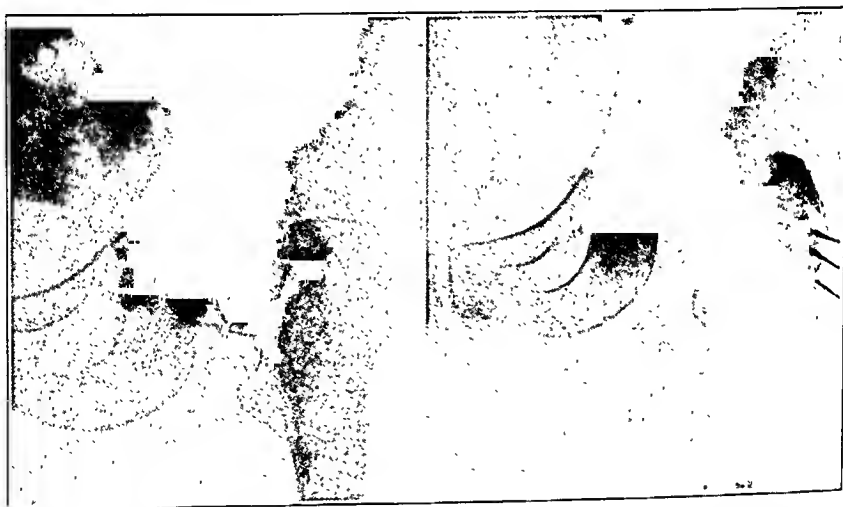


Fig. 38.—Fixation by means of several Kirschner wires. (From Telson and Ransohoff.) Picture on left, before reduction; picture on right, after first reduction and wiring.

10. No plaster bandage is applied, but a light pelvic brace is used. Baking and massage are instituted.

Earl D. McBride has adopted the use of the Whitman short spica with a Kirschner wire through the femoral condyles, incorporated in the plaster to give fixed countertraction. He described his method in 1933. Since then C. Percival Mills, of England, has described a similar method in the *Journal of Bone and Joint Surgery* of July 1935. He stated that the advantages of this method are: (1) easier reduction of the fracture and better control for the plaster of paris application; (2) greater comfort than is provided by the long spica; and (3) mobility of the knee and the ankle.

McBride has also used the Russell traction principle in cases in which confinement in plaster is not suitable.

Melvin Henderson, of the Mayo Clinic, in 1934 employed the blind nailing method, using the Kirschner wire as a guide. This procedure is similar to the method of Sven Johansson, as previously described, although it was devised independently and without knowledge of the existence of Johansson's method.



Fig. 39.—Method of taking lateral roentgenograms. A cassette is placed parallel with the longitudinal plane of the shaft of the femur. (From Johnson.)

Gaenslen in 1934 conceived the idea of inserting rustless steel fixation spikes, $\frac{3}{32}$ of an inch (0.3 cm.) in thickness, into the fragments subcutaneously at slight angles to one another (fig. 37). This is done with the affected leg abducted, at the level of the table, and internally rotated 10 to 15 degrees. Reduction of the fracture is obtained by

exertion of traction in the axis of the thigh, which is flexed at 90 degrees at the hip and knee. Then lateral pressure is applied over the trochanter and the leg is abducted to lock the fragments. Roentgenograms, anteroposterior and lateral, are taken. The spikes are introduced with the aid of hatpins around the greater trochanter for localization of the latter. Two Kirschner wires are drawn through the fragments to steady them.

Posterior plaster shells to both legs, previously prepared, are utilized to support the legs on pedestals while the anteroposterior and lateral roentgenograms are taken.

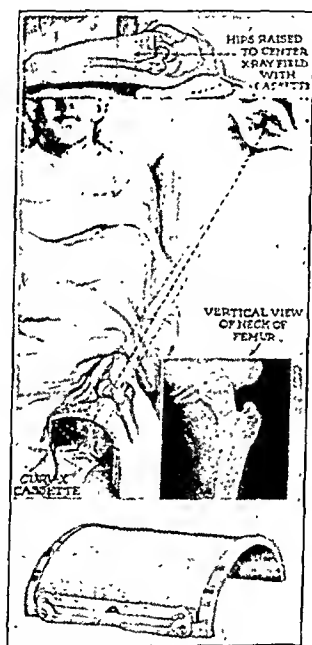


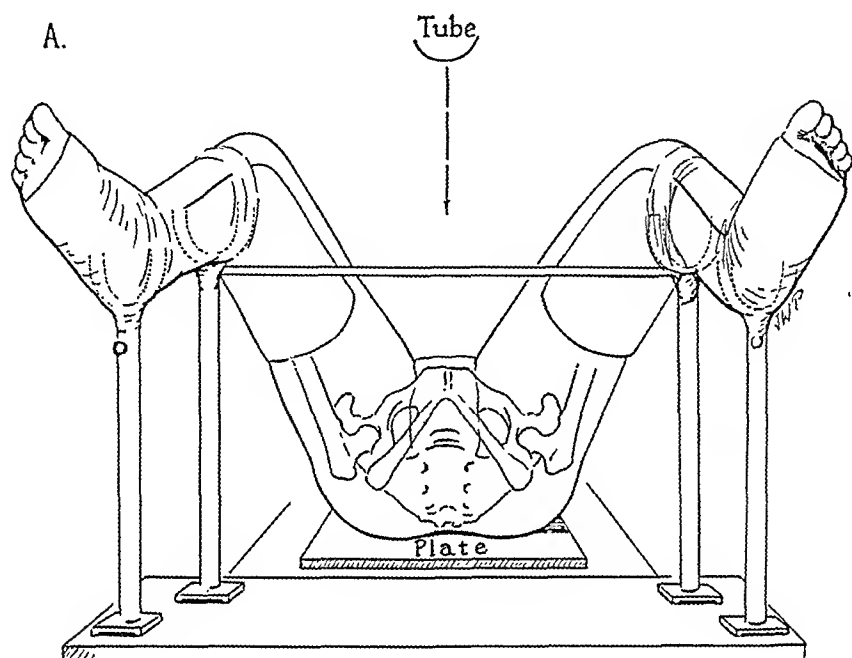
Fig. 40.—Method of taking lateral roentgenograms, with use of a specially adapted curved cassette. (From George and Leonard.)

Telson and Ransohoff (1932) likewise have utilized steel wires in their internal fixation operation (fig. 38). Kirschner wires are inserted subcutaneously at different angles. The point of entry and distance at which each wire is inserted are predetermined. The only apparatus used while the patient is in bed is a short posterior splint at the ankle to prevent external rotation, especially for obese persons. The patient is allowed to sit in a wheel chair within a day or so.

Carl P. Jones in 1932 introduced a Jones traction splint as an aid to extension of the affected limb. Plaster of paris boots are applied to both legs, and the traction splint is incorporated in these boots. Then the traction lever is turned until the desired effect is produced. It is

the author's claim that there is 20 pounds (9 Kg.) of pull on the traction apparatus per $\frac{3}{4}$ inch (1.9 cm.).

In March 1936 Snodgrass proposed a treatment based on the anatomic factors involved in this fracture. The principle that he advised was adduction and external rotation of the limb, maintained



B. Tracing from x-ray, obtained as above.

Lateral view showing angle of anterior torsion. Average about 12°

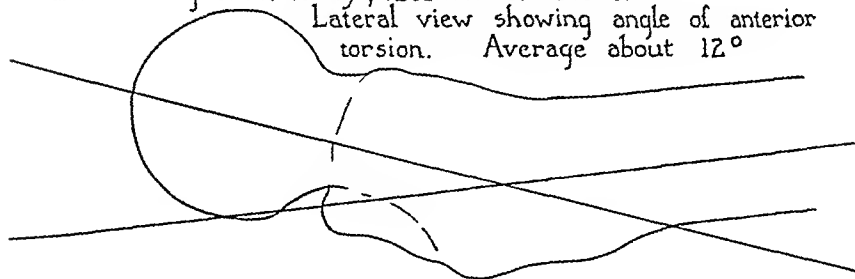


Fig. 41.—Another method of obtaining lateral roentgenograms. "Without moving the patient, it is possible to slip a plate under the buttocks and to obtain a lateral view of the affected hip." (Gaenslen.)

by a plaster spica. He reduced the fracture by traction, external rotation and anterior lifting of the thigh. He stated that after the fracture was reduced, the fascia lata, being placed on a tension by the adduction position of the limb, forcibly maintained impaction of the fragments by exerting constant pressure on the greater trochanter.

ROLE OF ROENTGEN RAYS

The advances made in the field of roentgenology have played an important part in the forward progress of the care of the "broken hip."

Tribute must be paid to Roentgen, who in 1895 introduced to the medical world the successful use of the x-ray apparatus. Added impetus was given by this new aid in the proper handling of these fractures.

At first the simple anteroposterior view was used exclusively. Of late years, however, the lateral roentgenogram has come into great vogue. This is largely because in many cases, although the anteroposterior film shows an apparently satisfactory apposition of the fragments, the lateral view shows a displacement, such as an open V anteriorly or posteriorly, or an end to side approximation; i. e., the fractured surface of the head fragment may lie against the posterior surface of the neck fragment, or vice versa.

In 1932 Clayton Johnson and George and Leonard at about the same time developed a technic for taking lateral views. They attained the same end in a different manner. Clayton Johnson placed a cassette (fig. 39) parallel with the longitudinal plane of the shaft of the femur, and the central rays projected from a point over the opposite thigh toward the affected hip joint at an angle of 25 degrees with the transverse plane of the femoral shaft. George and Leonard on the other hand (fig. 40), utilized a specially adapted curved cassette placed in the crotch, the central rays emanating from a point just to the side of the patient's head and directed toward the affected hip and cassette.

Gaenslen and O'Meara also contrived methods of their own (fig. 41) for obtaining lateral views.

SUMMARY

In this historical survey I have tried to trace the various methods employed in the treatment of transcervical fractures of the neck of the femur from the time of Ambroise Paré (1510-1590) to the present time. I have observed that the ancients (Hippocrates, Celsus, Galen, Avicenna and others) left no evidence of their knowledge of the existence of such a fracture. In his account Ambroise Paré brought attention to this fact very clearly. He pointed out how, in all probability, as he himself had been guilty of doing previously, physicians had wrongly diagnosed all such fractures and had treated them as dislocations of the hip.

If Ambroise Paré is to be accepted, then, as the first to recognize and distinguish fracture of the neck of the femur as a distinct surgical entity, the honor and credit of being the pioneer in the handling of this

most perplexing of fractures are due him. His attempt to treat the condition was crude and inefficient, consisting simply of applying splints and compresses with a hip spica bandage over them and about the affected hip joint. His aim, of course, was to maintain the fragments in place and immobilize the hip joint as much as possible.

It has been observed how the various fundamental principles in the treatment of fractures were applied; how new, specially adapted ones were discovered; how old ones were revived or modified, and how combinations of them were utilized. It is noted how one by one they were discarded, either because of ultimate failure or because of the suffering and discomfort experienced by the patient.

In reviewing the various methods, it is noted that many of them can be classified, e. g., splint immobilization, extension-counterextension, positions of semiflexion, abduction-internal rotation or adduction.

The following outline is an attempt to group these methods:

METHODS OF TREATMENT AND PRINCIPLES INVOLVED

I. Splints

1. Short splints maintained in place by a spica inguinalis bandage (Ambroise Paré, 1510-1590)
2. Desault splint-permanent extension
3. Thomas-Ridlon (1888), posterior hip brace
4. Bradford (1918) ambulatory abduction splint

II. Extension-counterextension methods

1. Girt of Fabricius Hildanus (1537-1619)
2. Jean-Louis Petit (1679-1750) extension-counterextension
3. Thomas ring splint with Buck's extension (1888)
4. Liston splint and Buck's extension
5. Well leg extension principle
 - (a) Brünigshausen?
 - (b) Gibson-Hagedorn Modification of Brünigshausen's method (1860)
 - (c) Wilkie splint (1927)
 - (d) Roger Anderson splint (1931)
 - (e) Jones traction splint (1932)

III. Semiflexion position with or without traction

1. Pott (1713-1788) Semiflexion position and no traction
2. Double inclined plane; no traction
(White, of Manchester, England, is said by Astley Cooper to have first advocated this.)
3. Sir Astley Cooper's method (1768-1841)—simply a pillow under the knee
4. Earle's bed (1828) principle of double inclined plane
5. N. R. Smith (1867) suspension splint
6. Russell traction (1924)

- IV. Principle of flexion at hip and knee
 - A. Applied in Reduction
 - 1. Dupuytren (1777-1835)
 - 2. Scudder
 - 3. Ruth (1891)
 - 4. Moore (1912)
 - 5. Leadbetter (1933)
 - 6. Gaenslen (1932)
 - B. Applied in Fixation
 - 1. J. A. Moore (1912), plaster abduction and flexion at the hip
 - 2. Gaenslen (1934), plaster abduction and flexion at hip plus internal spike fixation
- V. Principle of abduction
 - 1. Whitman (1904) abduction by the plaster of paris spica method
 - 2. E. H. Bradford (1918) abduction with ambulatory splint
 - 3. Russell traction (1924)
 - 4. Leadbetter (1933)
 - 5. Wilkie (1927)
 - 6. Roger Anderson (1931)
- VI. Principle of adduction
 - 1. Snodgrass (1936)
- VII. Distention
 - 1. Gooch (?-1780)
 - 2. Aitken (?-1790)
 - 3. Earle D. McBride (1933)
- VIII. Lateral pressure on greater trochanter
 - 1. Pott
 - 2. Desault
 - 3. Senn (1889)
 - 4. Scudder (at one time Scudder advocated Thomas-Ridlon splint with Senn's lateral pressure)
- IX. Impaction
 - 1. Cotton (1910)
 - 2. Smith-Petersen (1925)
- X. Lateral and longitudinal traction
 - 1. Maxwell (1871)
 - 2. Ruth (1891)
- XI. Multiple drill holes
 - 1. Bozsán (1932)
- XII. Dextrinized splint (hip spica bandage)
 - 1. Velpeau (1841)
- XIII. Plaster of paris bandage
 - 1. Senn (1889)
 - 2. Whitman (1902)

XIV. Internal fixation

1. Metal nail

- (a) Von Langenbeck (1858)
- (b) Koenig (1875)
- (c) Trendelenburg (1878)
- (d) Lister (1880)
- (e) Lemon (1913)
- (f) Smith-Petersen (1925) three-flanged nail
- (g) Wescott (1932)
- (h) Sven Johansson (1932)

2. Wires

- (a) Gaenslen (1932)
- (b) Telson and Ransohoff (1932)

3. Autogenous Bone Peg

- (a) Delbet (1911) fibular bone peg
- (b) Albee (1912) tibial bone peg
- (c) Ellis Jones dowel peg from greater trochanter

4. Screws

- 1. Delbet screw (1907)
- 2. Laurence Jones closed double screw (1933)
- 3. Myron Henry screw bolt (1934)

XV. No treatment (except sandbags)

CONCLUSION

In review, it may be seen that the evolution of the treatment of this type of fracture has been slow and arduous. New principles or devices seldom have been successful.

Improvements of any importance have been few and far between. It is only within the memory of many living surgeons, within the last thirty or forty years, that the greatest progress has been made in this field.

BIBLIOGRAPHY

- Aegineta, P.: *The Seven Books of Paulus Aegineta*, translated and edited by F. Adams, London, Sydenham Society, 1846, vol. 2, book 6, p. 466.
- Aitken, J.: *Essays on Fractures and Luxations*, London, T. Cadell & J. Murray, 1790.
- Albee, F. H.: *Autogenous Bone Peg as Primary Treatment for Fresh Fractures of Neck of Femur*, *California & West. Med.* **37**:1 (July) 1932.
- Bone-Graft Surgery*, Philadelphia, W. B. Saunders Company, 1915.
- Amesbury, J.: *A Syllabus of Surgical Lectures on the Nature and Treatment of Fractures, Diseases of the Joints, and Deformities of the Limbs and Spine*, London, T. & G. Underwood, 1827.
- Observations on the Nature and Treatment of Fractures of the Upper Third of the Thigh-Bone*, *ibid.*, 1828.
- Practical Remarks on the Nature and Treatment of Fractures of the Trunk and Extremities*, London, Longman [and others], 1831.
- Anderson, R.: *A New Method for Treating Fractures, Utilizing the Well Leg for Countertraction*, *Surg., Gynec. & Obst.* **54**:207 (Feb.) 1932.

- Bardenheuer: Behandlung der subcutanen Fracturen mittels Extension im Gegensatz zur Nahtanlegung und zum Contentiv-Verbände, *Arch. internat. de chir.* **1**:237, 1903.
- Basset, A.: Fractures et pseudo arthroses du col du fémur, in *L'oeuvre scientifique du Professeur Pierre Delbet*, Paris, Masson & Cie, 1932.
- Bell, B.: *A System of Surgery*, ed. 5, Edinburgh, Bell & Bradfute, 1791, vol. 6.
- A System of Surgery*, edited by N. B. Waters, Philadelphia, T. Dobson, 1806.
- Bell, C.: *Observations on Injuries of Spine and of the Thigh-Bone*, London, T. Legg, 1824.
- Bell, J.: *The Principles of Surgery*, Edinburgh, T. Cadell & W. Davies, 1801, vol. 1; 1806, vol. 2; 1808, vol. 3; edited by J. A. Smith, New York, Collins & Perkins, 1810, vol. 3.
- The Principles of Surgery as They Relate to Wounds, Ulcers, Fistulae, Aneurisms, Wounded Arteries, Fractures of the Limbs, Tumors, and the Operations of Trepan and Lithotomy*, London, T. Legg, 1826.
- Belloq: *A Description of a Machine for Oblique Fractures of the Shaft of the Femur and of Its Neck*, *Mém. Acad. roy. de chir.* **3**:233, 1778.
- Boyer, A.: *The Lectures of Boyer upon Diseases of the Bones*, edited by A. Richerand and translated by M. Farrell, London, J. Murray, 1804; edited by J. Hartshorne, Philadelphia, J. Humphreys, 1805.
- Traité des maladies chirurgicales et des opérations qui leur conviennent*, Paris, Ve. Migneret, 1814-1828.
- A Treatise on Surgical Diseases and the Operations Suited to Them*, translated by A. H. Stevens, New York, T. & J. Swords, 1815-1816, vol. 2.
- Buck, G.: *An Improved Method of Treating Fractures of the Thigh*, Illustrated by Cases, *Tr. New York Acad. Med.* **2**:233, 1861.
- Campbell, W. C.: *Central or Intracapsular Fractures of the Neck of the Femur*, *South. Surgeon* **2**:1 (March) 1933.
- Colles, A.: *Lectures on the Theory and Practice of Surgery*, edited by S. McCoy, Dublin, S. J. Machen, 1844-1845.
- Cotton, F. J.: *Artificial Impaction in Hip Fracture*, *Am. J. Orthop. Surg.* **8**: 680 (May) 1911.
- Cunningham, D. J.: *Cunningham's Text-Book of Anatomy*, edited by J. C. Brash and E. B. Jamieson, ed. 7, London, Oxford University Press, 1937.
- Da Costa, J. C.: *Modern Surgery, General and Operative*, ed. 8, Philadelphia, W. B. Saunders Company, 1919.
- Darrach, W., and Stimson, B. B.: *Displacements in Fractures of the Neck of the Femur*, *Ann. Surg.* **100**:833 (Oct.) 1934.
- Davis, G. G.: *Applied Anatomy: The Construction of the Human Body Considered in Relation to Its Functions, Diseases and Injuries*, ed. 9, Philadelphia, J. B. Lippincott Company, 1934.
- Davison, C., and Smith, F. D.: *Autoplastic Bone Surgery*, Philadelphia, Lea & Febiger, 1916.
- Delbet, P.: *Résultat éloigné d'un visage pour fracture transcervicale du fémur*, *Bull. et mém. Soc. de chir. de Paris* **45**:305, 1919.
- Faltin, R.: *The Treatment of the Fractures of the Neck of the Femur*, *Acta chir. Scandinav.* **57**:10, 1924.
- Fergusson, W.: *A System of Practical Surgery*, ed. 2, London, J. Churchill, 1846.
- Fowler, G. R.: *A Treatise on Surgery*, Philadelphia, W. B. Saunders Company, 1906, vol. 2.
- Gaenslen, F. J.: *Subcutaneous Spike Fixation of Fresh Fractures of the Neck of the Femur*, *J. Bone & Joint Surg.* **17**:739 (July) 1935.

- George, A. W., and Leonard, R. D.: Ununited Intracapsular Fractures of the Femoral Neck Roentgenographically Considered, *Am. J. Roentgenol.* **31**: 433 (April) 1934.
- Gibson, W.: *The Institutes and Practice of Surgery, Being the Outlines of a Course of Lectures*, ed. 6, Philadelphia, J. Kay Jr., 1841, vol. 1; ed. 8, 1850, p. 290.
- Gooch, B.: *Cases and Practical Remarks in Surgery*, London, D. Wilson & T. Durham, 1758, p. 122.
- Gray, H.: *Anatomy of the Human Body*, ed. 23, edited by W. H. Lewis, Philadelphia, Lea & Febiger, 1936.
- Hamilton, F. H.: *A Practical Treatise on Fractures and Dislocations*, Philadelphia, Blanchard & Lea, 1860.
- Heister, L.: *A General System of Surgery*, English translation, London, W. Innys [and others], 1743.
- Henderson, M. S.: Recent Fracture of the Hip: Smith-Petersen Nail Inserted Over Kirschner Wire, *Proc. Staff Meet., May Clin.* **9**:203 (April 4) 1934.
- Hickey, P. M.: Value of a Lateral View of the Hip, *Am. J. Roentgenol.* **3**: 308 (June) 1916.
- Hippocrates: *The Genuine Works*, translated and edited by F. Adams, London, Sydenham Society, 1849, vol. 2.
- Johansson, S.: An Operative Treatment of Medial Fractures of the Neck of the Femur, *Acta orthop. Scandinav.* **3**:362, 1932.
- Johnson, C. R.: A New Method for Roentgenographic Examination of the Upper End of the Femur, *J. Bone & Joint Surg.* **14**:859 (Oct.) 1932.
- Jones, C. P.: Intracapsular and Intertrochanteric Fractures of the Femur and Fractures of the Pelvis: Their Treatment, *California & West. Med.* **36**:79 (Feb.) 1932.
- Jones, E.: Trochanteric Transplantation in the Treatment of Fractures of the Neck of the Femur, *J. Bone & Joint Surg.* **14**:259 (April) 1932.
- Jones, L.: Intracapsular Fractures of the Neck of the Femur: A Closed Double-Screw Method for Reduction and Fixation; Preliminary Report, *Ann. Surg.* **97**:237 (Feb.) 1933.
- Keen, W. W.: *Surgery: Its Principles and Practice*, Philadelphia, W. B. Saunders Company, 1907, vol. 2.
- King, M. J.: Recent Intracapsular Fractures of the Neck of the Femur: A Critical Consideration of Their Treatment and a Description of a New Technique, *M. J. Australia* **1**:5 (Jan. 6) 1934.
- Kolodny, A.: The Architecture and Blood Supply of the Head and Neck of the Femur and Their Importance in the Pathology of Fractures of the Neck, *J. Bone & Joint Surg.* **7**:575 (July) 1925.
- Langan, A. J.: The Use of the Jones Splint in the Treatment of Fractures of the Pelvis and of the Neck of the Femur, *J. Bone & Joint Surg.* **17**:435 (April) 1935.
- Leadbetter, G. W.: A Treatment for Fracture of the Neck of the Femur, *J. Bone & Joint Surg.* **15**:931 (Oct.) 1933.
- Leveuf, J. B.; Girode, C., and Monod, R. C.: *Traitement des fractures et luxations des membres*, ed. 2, Paris, Masson & Cie, 1935.
- Löfberg, O.: Treatment of Fractures of the Neck of the Femur, *Acta chir. Scandinav.* **57**:504, 1924.
- McBride, E. D.: *Disability Evaluation: Principles of Treatment of Compensable Injuries*, Philadelphia, J. B. Lippincott Company, 1936.

- McGlannan, A.: Fracture of the Neck of the Femur: A Study of the Treatment and End Results in Fifty-Five Cases, *Surg., Gynec. & Obst.* **22**:287 (March) 1916.
- Malgaigne, J. F.: A Treatise on Fractures, translated by J. H. Packard, Philadelphia, J. B. Lippincott & Co., 1859.
- Maxwell, T. J.: Fracture of the Neck of the Femur, *Chicago M. J. & Exam.* **33**:401, 1876.
- Morgagni, J. B.: The Seats and Causes of Diseases Investigated by Anatomy, abridged edition translated by B. Alexander and edited by W. Cooke, London, Longman [and others], 1822.
- Ochsner, E. H., and Sullivan, J. K.: Recent Fractures of the Hip, *Internat. J. Med. & Surg.* **42**:620 (Dec.) 1929.
- O'Meara, J. W.: Fractures of the Femoral Neck Treated by Blind Nailing, *New England J. Med.* **212**:43 (Jan. 10) 1935.
- Paré, A.: Works, translated by T. Johnson, London, T. Cotes & R. Young, 1634.
- Petit, J. L.: Treatise on Diseases of the Bones, London, T. Woodward, 1776.
- Phemister, D. B.: Fractures of the Neck of the Femur, Dislocations of the Hip and Obscure Vascular Disturbances Producing Aseptic Necrosis of the Head of the Femur, *Surg., Gynec. & Obst.* **59**:415 (Sept.) 1934.
- Phillips, G. W.: Fracture of the Neck of the Femur: Treatment by Means of Extension with Weights, Applied Both in the Direction of the Axis of the Limb, and Also Laterally in the Axis of the Neck, *Am. J. M. Sc.* **58**:398 (Oct.) 1869.
- Pott, P.: The Chirurgical Works of Percival Pott, from the English edition by J. Earle, Philadelphia, J. Webster, 1819.
- Ridlon, J.: Double Hip Disease: A Report of Fourteen Consecutive Cases, with Conclusions, *Tr. Am. Orthop. A.* **1**:276, 1889.
- Russell, R. H.: Fracture of the Femur: A Clinical Study, *Brit. J. Surg.* **11**:491 (Jan.) 1924.
- Ruth, C. E.: Fractures of the Femoral Neck and Trochanters: A Rational Treatment, *Tr. Sect. Orthop. Surg., A. M. A.*, 1921, p. 163; *J. A. M. A.* **77**:1811 (Dec. 3) 1921.
- Scudder, C. L.: The Treatment of Fractures, ed. 6, Philadelphia, W. B. Saunders & Co., 1907, p. 343.
- Scultetus, J.: *Armentarium chirurgicum bipartitum*, Frankfurt, sumpt. vid. J. Gerlini, 1666.
- The Chyrurgeons Store-House, English translation, London, J. Starkey, 1674.
- Senn, N.: Practical Surgery for the General Practitioner, Philadelphia, W. B. Saunders & Co., 1901.
- Shaffer, N. M.: Selected Essays on Orthopedic Surgery, New York, J. P. Putnam's Sons, 1923.
- Smith, N. R.: Treatment of Fractures of the Lower Extremity by the Use of the Anterior Suspensory Apparatus, Baltimore, Kelly & Piet, 1867.
- Smith-Petersen, M. N.: Treatment of Fractures of the Neck of the Femur by Internal Fixation, *Surg., Gynec. & Obst.* **64**:287 (Feb. 15) 1937.
- Cave, E. F., and Vangorder, G. W.: Intracapsular Fractures of the Neck of the Femur: Treatment by Internal Fixation, *Arch. Surg.* **23**:715 (Nov.) 1931.
- Speed, K.: The Unsolved Fracture, *Surg., Gynec. & Obst.* **60**:341 (Feb. 15) 1935.
- A Text-Book of Fractures and Dislocations Covering Their Pathology, Diagnosis and Treatment, ed. 3, Philadelphia, Lea & Febiger, 1935.

- Stimson, L. A.: *A Practical Treatise on Fractures and Dislocations*, ed. 8, Philadelphia, Lea & Febiger, 1917.
- Telson, D. R., and Ransohoff, N. S.: Treatment of Fractured Neck of the Femur by Axial Fixation with Steel Wires, *J. Bone & Joint Surg.* **17**: 727 (July) 1935.
- Thomas, H. O.: Fractures, Dislocations, Deformities and Diseases of the Lower Extremities, in *Contributions to Surgery and Medicine*, London, H. K. Lewis, 1890, pt. 7, p. 55.
- Velpeau, A. A. L. M.: *Leçons orales de clinique chirurgicale faites à l'Hôpital de la Charité*, collected by G. Jeanselme, Paris, Germer-Baillière, 1841, vol. 2, p. 552.
- Watson-Jones, R.: Fractures of the Neck of the Femur, *Brit. J. Surg.* **23**: 787 (April) 1936.
- Wescott, H. H.: Preliminary Report of a Method of Internal Fixation of Transcervical Fractures of the Neck of the Femur in the Aged, *Virginia M. Monthly* **59**:197 (July) 1932.
- A Method for the Internal Fixation of Transcervical Fractures of the Femur. *J. Bone & Joint Surg.* **16**:372 (April) 1934; *South. Med. & Surg.* **96**:458 (Sept.) 1934.
- End-Results After Internal Fixation of Transcervical Fractures of the Femur, *Virginia M. Monthly* **62**:446 (Nov.) 1935.
- White, J. W.: Instrument Facilitating the Use of the Flanged Nail in Treatment of Fractures of the Hip, *J. Bone & Joint Surg.* **17**:1065 (Oct.) 1935.
- Whitman, R.: A New Treatment for Fracture of the Neck of the Femur, *M. Rec.* **65**:441 (March 19) 1904.
- Wilkie, D. P. D.: A New Treatment for Fracture of the Neck of the Femur, *Surg., Gynec. & Obst.* **44**:529 (April, pt. 1) 1927.
- Wilson, P. D., and Cochrane, W. A.: *Fractures and Dislocations*, ed. 2, Philadelphia, J. B. Lippincott Company, 1928.

ARTERIAL OCCLUSION WITH ASEPTIC NECROSIS OF BONE

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CHICAGO

An adequate blood supply is necessary for the nutrition of bone tissue. Complete interruption of the circulation causes infarction or aseptic necrosis.¹ The extent of such a circulatory disturbance determines the amount of necrosis in a bone, although impeded or interrupted circulation does not affect equally all bone tissue. According to Haslhofer,¹ Axhausen and Bergmann¹ and Müller,² diminished blood supply causes necrosis of portions of the bone tissue while the marrow structures remain intact. The statements of these authors emphasized that bone as a tissue is readily damaged by obstruction of the circulation, a view in marked contrast with the older opinion that the great vascularity of bones precludes infarction. Burckhardt³ shared this view and concluded that excessive stress of the bands carrying the nutrient vessels to bones or a direct break in the continuity of the nutrient blood supply would cause a serious local injury of the bone. He observed the formation of new bone only when the marrow and periosteum were injured. Damage to the periosteum and marrow, he stated, constitutes a stimulus to regeneration rather than to necrosis of the ground substance of the bone. The vessels supplying blood to the diaphyses of long bones are, according to Johnson,⁴ in the order of their importance: (1) nutrient vessels piercing the cortex, which maintain the viability of the medulla and supply the inner half of the cortex; (2) metaphysial

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1. The comprehensive reviews by G. Kistler (Sequences of Experimental Infarction of the Femur in Rabbits, *Arch. Surg.* **29**:589 [Oct.] 1934; Effects of Circulatory Disturbances on the Structure and Healing of Bone: Injuries of the Head of the Femur in Young Rabbits, *ibid.* **33**:225 [Aug.] 1936) and those published more recently by L. Haslhofer (in Henke, F., and Lubarsch, O.: *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1937, vol. 9, pt. 3) and G. Axhausen and E. Bergmann (in Henke, F., and Lubarsch, O.: *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1937) contain most of the important literature references on this subject.

2. Müller, W.: *Beitr. z. klin. Chir.* **138**:614, 1927.

3. Burckhardt, H.: *Beitr. z. klin. Chir.* **138**:625, 1927.

4. Johnson, R. W., Jr.: *J. Bone & Joint Surg.* **9**:153, 1927.

vessels, which penetrate the cortex to supply the marrow and the inner half of the cortex, and (3) periosteal vessels, which nourish the outer half of the cortex and have a limited capacity as a source of collateral circulation.

The fate of bone aseptically necrotic because of disturbances in circulation varies considerably. According to Phemister,⁵ when the necrotic bone is closely united with living bone, fibrous and osteogenic tissues grow from the living into the necrotic bone, and by creeping substitution the old bone is gradually absorbed and replaced by new bone. The degree of restitution, he stated, depends on several factors, such as functional stimulation, anatomic location and the quantity of contiguous living bone. To these should be added adequacy of the blood supply and ability of the tissues to revascularize the dead portions. A comprehensive summary by Rohde⁶ emphasized the importance of the role of the vascular system in the entire process of bone regeneration. The intactness of the blood supply and the ability of the blood to react, he stated, determine regeneration. When the circulation is maintained, the fracture hyperemia persists sufficiently, and bone regeneration occurs from surviving osteoblasts. Damage of the blood supply by the initial injury or subsequently in the process of regeneration results in a growth of scar tissue at the expense of bone, from the constituents of the bone or from the surrounding tissues. Complications of the restitution process develop when functional activity causes impression or compression fractures of the bone tissues affected and additional injury to the nutrient arteries or their intrinsic branches.

Disturbances in nutrition are accepted generally as the cause of aseptic necrosis of bone. Various opinions have been expressed, however, concerning the cause of such disturbances (except those produced by chemicals, by irradiation, or by some other obvious specific cause). In an argumentative analysis of the pathogenesis of nonspecific aseptic necrosis (spongiosa disease) of bone, Block⁷ concluded that vascular disturbances account for only a few lesions. More probably, he argued, the nutritional disturbances depend on colloidal and chemical alterations of the spongiosa, changes in the blood vessels being incidental. Block conceded that vascular occlusion would provide the simplest explanation for the nutritional disturbances but stated that he is unacquainted with evidence of occluded or narrowed blood vessels. Haslhofer¹ regarded ischemia as the fundamental factor in causation of nonspecific aseptic necrosis of bones, but the cause of this vascular interference is not clear. He considered Axhausen's theory of embolic infarction improba-

5. Phemister, D. B.: *J. Bone & Joint Surg.* **12**:769, 1930.

6. Rohde, C.: *Arch. f. klin. Chir.* **123**:530, 1923.

7. Block, W.: *Arch. f. klin. Chir.* **174**:172, 1933.

ble and supported the opinion of Kienbock, who concluded that nutrient vessels of bones are injured by trauma often considered insignificant by the patient. Cordes⁸ concluded that aseptic necrosis of the os lunatum of the wrist always is due to a fracture, the extent of necrosis being dependent on the severity of the injury. Legg-Perthes' disease and aseptic necrosis of other bones, he stated, are caused by interruption of the blood supply. There can be no sharp distinction between the two processes, for when fracture occurs, blood vessels are injured; and the extent of damage to them, as Rohde emphasized, determines largely the subsequent healing processes. Novotny⁹ considered circulatory disturbances the most important cause of aseptic necrosis of the metatarsal bones (Köhler's disease). Such disturbances occur, he stated, when unusual movements or traumas injure the nutrient arteries carried in the collateral bands of the metatarsophalangeal joint and thus interrupt the blood supply to the head of the metatarsal bone.

Although many authors accept disturbances in nutrition as fundamental in aseptic necrosis of bones, the basic factors causing such a disturbance seem to have been postulated rather than subjected to study. Axhausen's theory of embolic infarction is attractive, yet the demonstration of such vascular occlusions in the human being has not been accomplished. Supporting evidence has been found, however, in experiments on animals.¹ Block, conceding the simplicity of vascular occlusion as a cause for aseptic necrosis of bone, said that he was unacquainted with evidence of occluded or narrowed blood vessels. Perhaps opportunities to study changes in nutrient arteries leading to regions of aseptically necrotic bone tissue have been disregarded or not fully utilized. Occlusions or constrictions of nutrient arteries associated with aseptic necrosis of bone tissues, however, are the main theme of this report.

REPORT OF CASES

CASE 1.—A white man, aged 54, a crane operator, entered St. Luke's Hospital on Nov. 26, 1937, because of pain and limited mobility of the left wrist. On August 7 he had fallen about 30 feet (9 meters) to the ground. Among other injuries was a fracture of the left wrist. After one week in a splint the left wrist was incised and a bone was removed. On November 27 pieces of articular cartilage and cancellous bone were removed through an incision of the old scar. The report on a roentgenogram taken on November 29 recorded the loss of parts of some of the small bones of the wrist and a dislocation of the semilunar bone. This bone was removed by Dr. Harry E. Mock on December 7. It was 2.5 by 2 cm. across the convex articular surface and was 1.8 cm. thick. The cartilage of the concave articular surface was glistening; that of the convex surface had lost its smoothness, and the bone tissues beneath were friable.

8. Cordes, E.: *Beitr. z. klin. Chir.* 149:28, 1930.

9. Novotny, O.: *Arch. f. klin. Chir.* 190:604, 1937.

The bone was fixed in Zenker's solution, hemisected and embedded in pyroxylin. The sections, stained with hematoxylin and eosin, were examined for changes in the large nutrient arteries. A large nutrient artery in one block entered the bone tissues in a mass of edematous scar tissue. The original lumen (fig. 1 *A*) was reduced to a narrow slit by an intimal thickening of fibroblastic tissue containing a

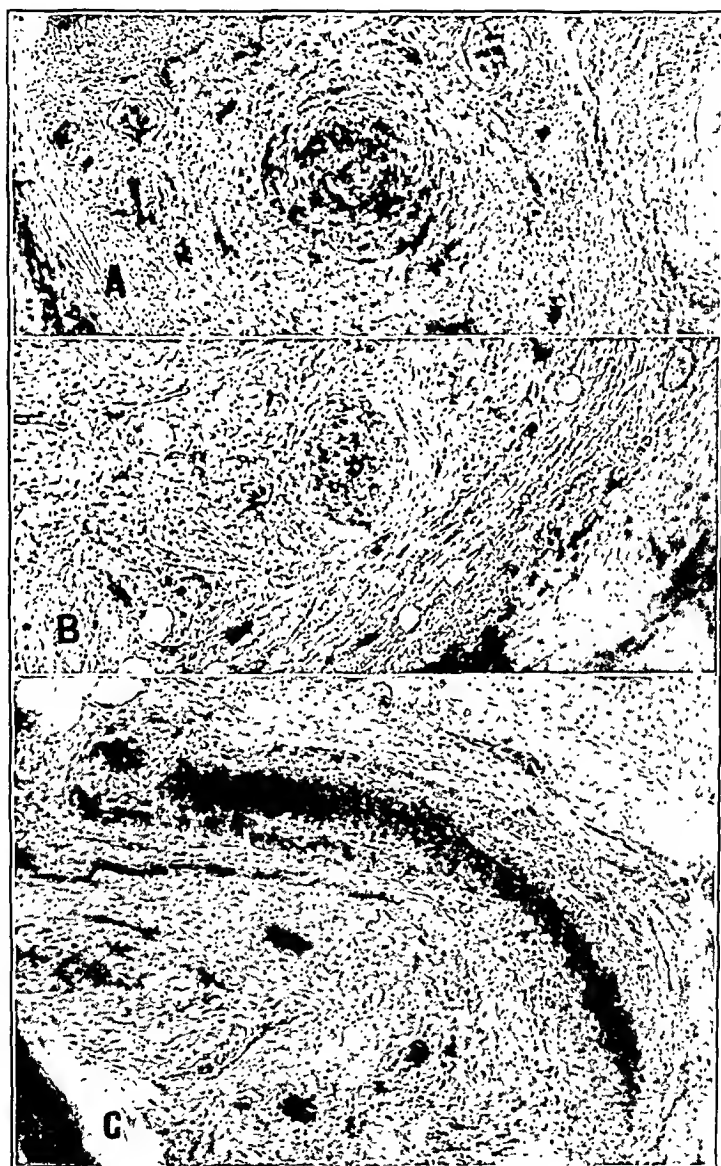


Fig. 1.—*A*, photomicrograph ($\times 88$) illustrating the fibrous tissue thickening of the intima and obliteration of the lumen of a nutrient artery extending into the lunate bone (case 1). *B*, photomicrograph ($\times 88$) of a branch of a nutrient artery with a thickened wall and a small lumen, embedded in fibrous tissues that have replaced portions of the bone (case 1). *C*, photomicrograph ($\times 88$) of a nutrient artery extending into the lunate bone, illustrating the fibrous tissue thickening of the wall and the greatly reduced lumen (case 2).

few polymorphonuclear leukocytes. The walls of several small arterial branches (fig. 1 *B*) at other levels in this fibrous tissue showed similar changes. The marrow fat was mixed with fibrous tissue. The articular cartilage was intact, but beneath it were broken fragments of necrotic bone trabeculae. There was no reactive bone tissue. The artery channels deep in the bone showed dilated lumens filled with blood cells. The marrow fat was extensively replaced by fibrous tissue.

CASE 2.—A white man aged 37, a laborer, entered St. Luke's Hospital on Dec. 7, 1937, because of pain and flexion immobility of the left wrist. On March 13, his left hand, slipping on a pump handle, had been forced into sharp dorsal extension. Flexion of the wrist and the stress of a weight caused pain. Three weeks before his admission, a roentgen examination demonstrated a volar dislocation of the os lunatum. Dr. W. R. Cubbins explored the tissues on the day of the patient's admission to the hospital and removed the dislocated bone because it could not be replaced. The convexly curved articular surface was 2.3 by 1.8 cm. The thickness of the bone was 1.7 cm. The cartilage of both articular surfaces had lost the usual gloss, and portions were roughened by fibrous tissue.

The marrow fat was replaced by fibrous tissue. Large portions of the bone, cartilage and marrow tissue were necrotic. A large nutrient artery had thick fibrous walls and a compressed, narrow lumen (fig. 1 *C*). Arterial branches with constricted lumens were embedded in dense scar tissue.

CASE 3.—A white man aged 41 entered St. Luke's Hospital on Jan. 18, 1937, because of a swollen, painful left wrist. On Oct. 7, 1936, a package of newspapers had been thrown to him, the impact hyperextending his left hand. The hand could be flexed but not extended at the wrist. Lateral flexion was slight; medial flexion was absent. Roentgen examination disclosed necrosis of part of the os naviculare. Dr. Charles Drucek Jr. removed the bone on January 8. It was irregular, 2.5 by 1.5 by 1.3 cm., with portions broken away. The broken surface, mainly on one end, was 1.5 by 1.2 cm. The surface of the articular cartilage was smooth and glistening. Two other pieces of bone were 1.2 by 1 by 0.8 cm. and 1 by 0.8 by 0.6 cm. respectively.

The articular cartilage had the usual structure. The bone tissue beneath showed no changes, except the portion which showed decreased density in the roentgenogram (fig. 2 *A*). This was necrotic. The narrow spaces along the margins of this region contained edematous fibrous and fatty tissue. Deep in the marrow tissue and extending toward the necrotic region was a large nutrient artery with thick, muscular walls. The lumen of this vessel (figs. 2 *B* and 2 *C*), traced in interrupted serial sections, contained a fibroblastic tissue thrombus that filled all but a narrow edge of the lumen.

CASE 4.—A white man aged 27 fell on his extended right hand on Dec. 12, 1933. His wrist became swollen and painful. Partial immobilization gave no relief. He continued to work, but with discomfort; at times, pain at night was sufficient to keep him awake. Flexion and extension of the right wrist were considerably restricted; pronation and supination, slightly. Roentgen films disclosed fragmentation of the os lunatum. On Sept. 30, 1934, Dr. W. F. Lyon removed the lunate bone in several pieces. It was misshapen; it measured 1.2 by 1 cm. and was 1.6 cm. thick.

The concave articular surface had a narrow edge of hyaline cartilage. The flattened convex edge was covered by dense fibrous tissue; only a few small masses of hyaline cartilage remained. Dense fibrous tissue replacing portions of the bone contained many broken and necrotic fragments of bone trabeculae (fig. 2 *D*). There

was a slight reaction about some of the cartilage and bone fragments. The marrow spaces of the bone adjacent to the scarred portions contained edematous fibrous tissue or fibrous and fatty tissue. The nutrient arteries and their branches had small lumens and thick muscular and fibrous walls.

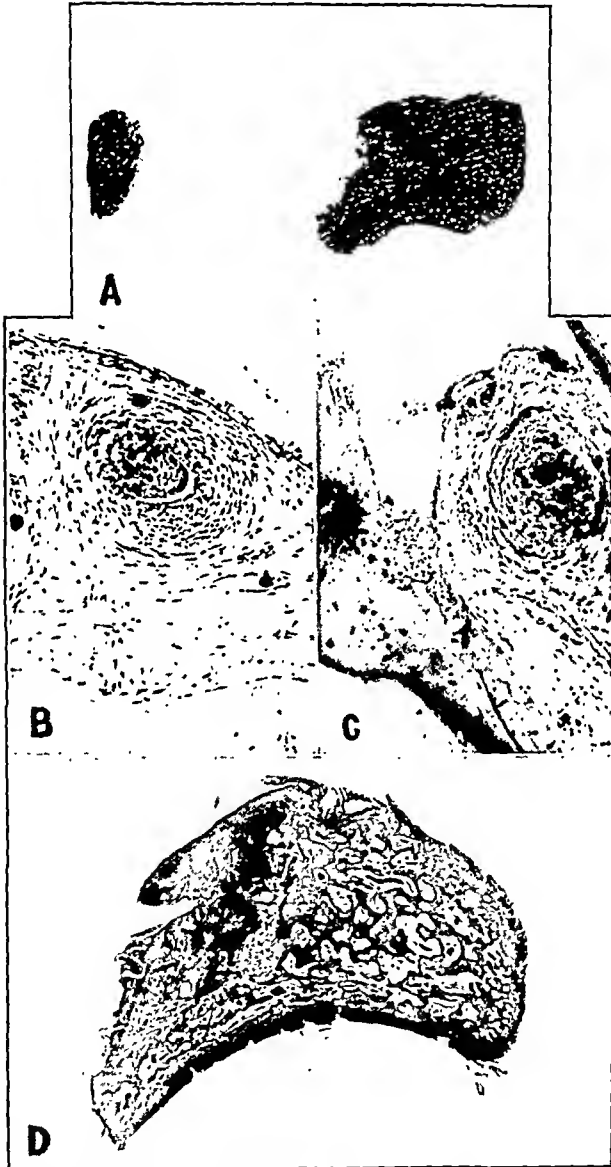


Fig. 2.—*A*, roentgenogram of the excised os naviculare, illustrating the changes in osseous texture (case 3). *B*, photomicrograph ($\times 88$) illustrating the organizing thrombus in a branch of a nutrient artery at the edge of the necrotic bone tissues (case 3). *C*, photomicrograph ($\times 88$) of one of the interrupted serial sections, illustrating the occluding thrombus at a level where it contained erythrocytes, leukocytes and organizing granulation tissue (case 3). *D*, photomicrograph ($\times 88$) of a section of the os lunatum, illustrating the necrotic portions and the portions replaced by fibrous tissue (case 4).

CASE 5.—A white youth aged 16 had been in excellent health until six months before his admission to St. Luke's Hospital on March 31, 1937. At that time he had fatigue and weakness of the left thigh, symptoms which he thought appeared after he had been kicked in this region. At the time of the presumed accident the

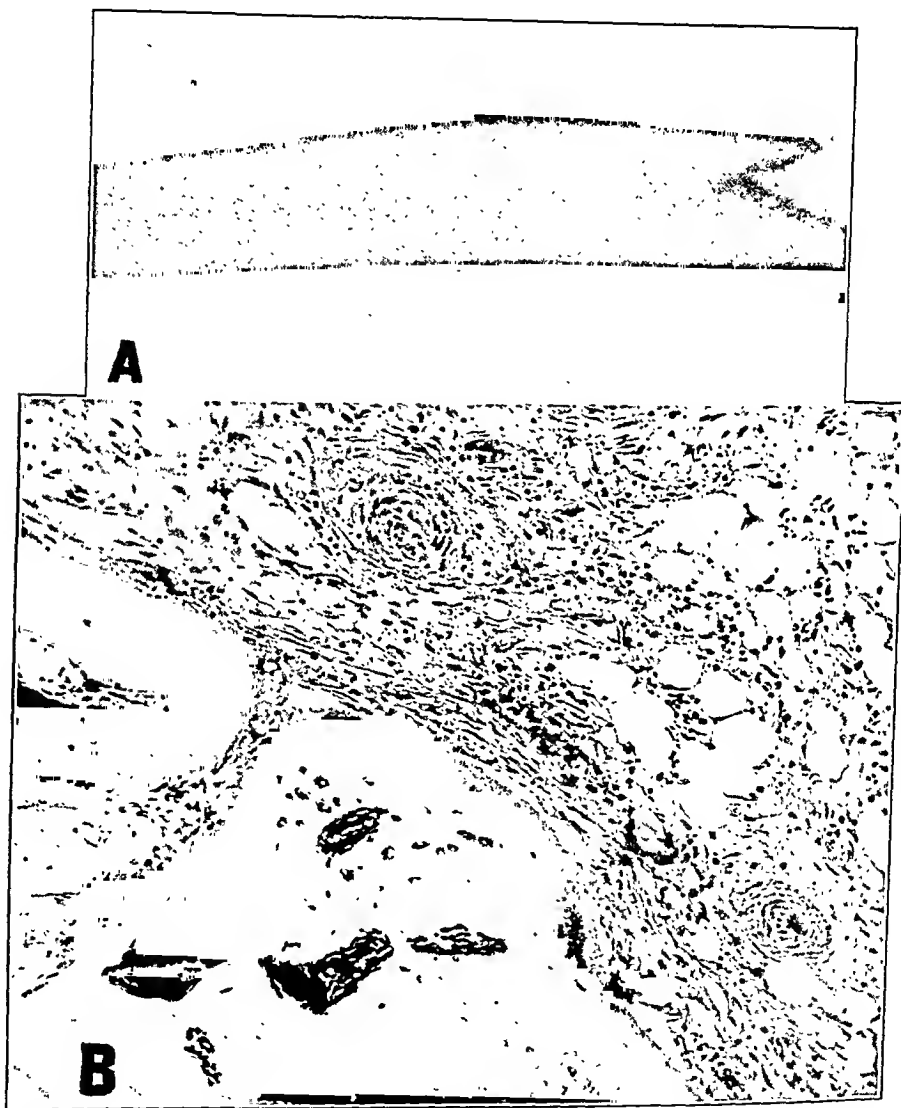


Fig. 3.—*A*, roentgenogram illustrating the thickening of the cortex of the shaft of the femur (case 5). *B*, photomicrograph ($\times 124$) illustrating the fibrous tissue invasion of the medullary tissues, arterioles with small lumens, and bone. Some necrotic trabeculae had new bone deposited along the margins (case 5).

tissues were not discolored or painful. After three months he had sharp pains in the middle of the left thigh, which radiated to the ankle and at night were sometimes severe enough to keep him awake. A slight limp developed. Roentgenograms (fig. 3 *A*) of the thigh disclosed thickening of the cortex above the middle of

the femur. Some regarded this thickening to be due to low grade osteomyelitis or to a neoplastic growth. On April 1 Dr. W. R. Cubbins exposed the cortex of the femur opposite the junction of the upper and middle thirds of the bone. The surface was roughened and elevated for about 8 cm. by sclerotic bone. The bone



Fig. 4.—*A* and *B*, photomicrographs ($\times 103$) illustrating the fibrous tissue thickening of the wall and collapse of the lumen of a nutrient artery associated with the bone lesion (case 5).

tissue was sclerotic and pale; the periosteum was intact and easily detached. After the thickened cortex had been removed, the marrow was found to be soft red tissue. Cultures of this tissue were sterile. The cortex of the medial side of the bone was pale and more dense than normal.

The marrow tissues removed contained necrotic bone trabeculae, some with margin layers of newly formed compact bone (fig. 3). The fat in the marrow spaces was replaced by fibrous tissue. Branches of the nutrient arteries had thick walls and small lumens. Some of the trabeculae of the cortex were necrotic,

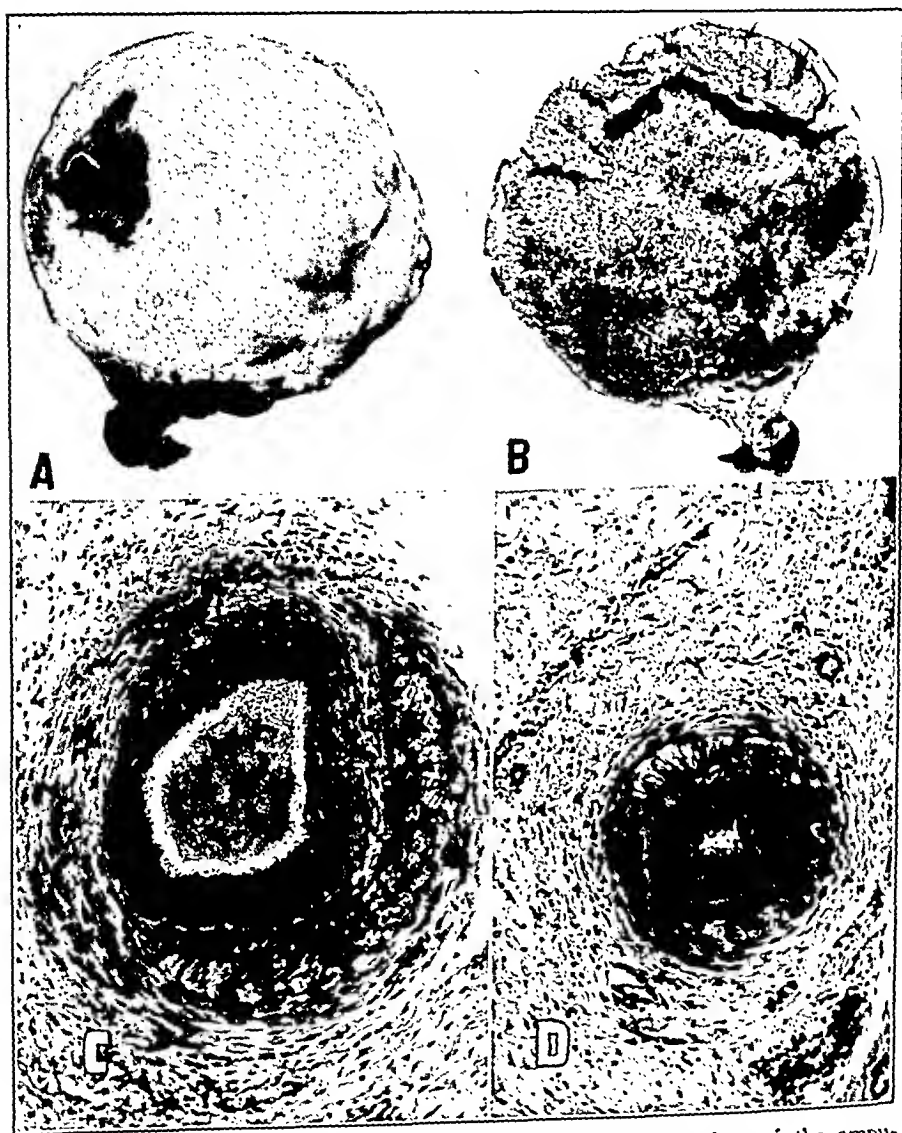


Fig. 5.—*A*, photograph illustrating the uneven articular surface of the amputated head of the femur (case 6). *B*, photograph of the surface made in amputating the head of the femur. Note the deep crevices and the sclerosed spongy bone (case 6). *C* and *D*, photomicrographs ($\times 105$) illustrating the intimal fibrous tissue thickenings of the nutrient arteries in the ligamentum teres (case 6).

and the marrow spaces contained fibrous tissue. Tissue of special interest was taken from the margin of the bone. It contained masses of differentiated bone callus. Embedded in scar tissue was a large nutrient artery (fig. 4) with a thick wall and a compressed, narrow lumen.

CASE 6.—A white man aged 44 had pain in the left hip and knee intermittently for eleven months. He walked with a limp, favoring the left leg because of pain. There was no limitation in the motion of the left hip or knee. Extreme flexion or abduction of the left thigh caused pain in the hip joint and inner surface of the thigh. The Wassermann reaction of the blood serum was negative. Dr. E. L. Jenkinson noted in roentgen films taken Dec. 3, 1932, rarefaction of the head of the femur and depression of a portion of the upper and outer half. He considered these portions of the bone necrotic. On December 14 Dr. Fremont A. Chandler¹⁰ exposed the left hip joint. He removed a dark red, swollen ligamentum teres, the head of the femur and a portion of the neck of the femur. Blood-stained fluids in the hip joint were sterile on culture. No further destruction of the proximal third of the femur was noted in a roentgenogram taken on July 12, 1933.

The amputated head of the left femur (figs. 5A and 5B) was hemispherical and measured 5.5 cm. in diameter. The surface made by the amputation was slightly concave; the thickness was about 2 cm. The fovea, 1 cm. from one edge, was 1.7 by 1.4 cm. The articular cartilage around this was elevated slightly, and about four fifths was pale gray-yellow and slightly granular. The cartilage was compressible. The surface made by amputation of the femoral head had a zone of condensed spongiosa along the periphery, 1.5 cm. wide. The sclerosed bone near the center contained yellow fat mottled with chalklike deposits 1 mm. in diameter. A crevice 1 to 3 mm. deep extended diagonally across the bone beneath the yellow, discolored articular cartilage.

The ligamentum teres, a pear-shaped mass of edematous fibrous tissue flattened on one side and rounded on the other, was 4 cm. long and 2.5 by 1.3 cm. at the broad end. The narrow end, measuring 0.7 by 0.4 cm., was attached to the fovea of the femur. A friable, necrotic region 1.5 by 0.8 by 0.8 cm. in the ligament was 1.8 cm. from the attachment of the femur. Some of the remaining edematous tissue was hemorrhagic.

A segment of bone 8 mm. thick, cut from the amputated head of the femur in a plane through the fovea capitis, was fixed in Zenker's solution, decalcified and embedded in pyroxylin, and the sections were stained with hematoxylin and eosin. A broad piece of articular cartilage with attached necrotic bone formed the roof of the large crevice, 2 to 7 mm. wide. Laterally, where the crevice reached the cartilage there was only a narrow bridge of cartilage or fibrous tissue. The bone trabeculae about this crevice were necrotic. The marrow spaces contained granular tissue débris and small fragments of necrotic bone (bone dust). Distal to the crevice this necrotic bone tissue extended variably to a depth of 8 mm. It merged into bone with marrow spaces containing edematous, poorly cellular fibrous tissue alone or with fat. There were small focal infiltrations of plasma cells and lymphocytes, but no reactive bone tissue was observed. The tissue of the ligamentum teres was edematous and hemorrhagic. Portions, as has been stated, were necrotic. A fibroblastic tissue reaction with chronic inflammatory exudates, recent hemorrhages and edema were the essential changes. There were many large and small arteries. These had thick muscular and fibrous walls and small lumens (figs. 5C and 5D).

CASE 7.—A white man aged 33 had pain and stiffness of both hips, especially the left, for three years. The pain was accentuated in the morning and when he walked. A waddling limp developed. This, associated with the pain, made walking difficult. The symptoms referable to the left hip were more marked than those

10. The clinical and pathologic disorders of the patients in cases 6 and 7 were reported by Dr. Chandler (*Wisconsin M. J.* 35:585, 1936).

referable to the right. According to statements in the clinical record, this patient had carried heavy loads of meat on his shoulders. A diagnosis of aseptic necrosis of the head of each femur was made. Dr. Fremont A. Chandler reconstructed the left hip and removed the head of the femur on Dec. 26, 1934.

The cone-shaped head of the femur (fig. 6 *A* and 6 *B*), including a portion of the neck, was 6 by 5.5 cm. at the broken base and 5.5 cm. high. The articular surface was rough and extended to within 2.2 cm. of the broken surface at the base. This surface consisted of finely porous sclerosed bone. The irregular head was rounded abruptly at the tip. The fovea was an irregular depression 2 by 1.3 cm. and 0.9 cm. deep. A lip of bone tissue 8 mm. wide and 9 mm. long extended from the upper edge. A narrow, rounded, slightly overhanging lip on the opposite edge extended 12 mm. The articular surfaces were uneven, and portions were covered by fibrous tissue. A mass of cartilage 3 by 5.5 cm. with an uneven surface and loosened from the bone tissues was about 2 cm. below the prominent overhanging lip of the fovea. The hyperemic ligamentum teres was 5 cm. long and had been avulsed from the fovea of the femur with a piece of cartilage and fibrous tissue 1 by 1 by 0.2 cm. The ligament at the foveal attachment was 1.2 by 0.6 cm. and widened to 2 by 1.3 cm. at the acetabular end. The tissues were hemorrhagic. A "joint body" composed of two nodules held together closely was 1.5 by 0.8 by 0.3 cm.

The head of the femur was fixed in solution of formaldehyde, and two segments, each 7 mm. thick, were removed, one through the fovea and the other directly in front (fig. 6 *C*). They were decalcified and embedded in pyroxylin, and the sections were stained with hematoxylin and eosin. The overhanging lip (fig. 6 *D*) had a thin surface of articular cartilage and consisted mainly of bone trabeculae varying considerably in width. The small marrow spaces contained fat, alone or with fibrous tissue. Several pockets distributed in the peripheral portions of the head ranged to 1 cm. in diameter. They contained necrotic tissue débris and edematous fibrous or dense scar tissue. The bone trabeculae around these were not arranged regularly. Otherwise the structure of the bone varied mainly in density. Portions under the fovea and the displaced articular cartilage were compact; those near the neck approached the structure of the usual spongiosa. At some levels the large lip of the fovea had a second layer of cartilage beneath a thin plate of bone near the surface.

The ligamentum teres was sectioned at levels according to a sketch. It consisted mainly of fibrous tissue, dense near the center and less compact toward the periphery. There were a few recent hemorrhages. The blood vessels had thick muscular and fibrous walls. The lumens were small, and some of the large arterial branches showed fibrous tissue thickening (fig. 6 *E*) of the intima, which reduced the lumens to small slits or crevices.

CASE 8.—A white woman aged 55 had pain in the right hip and knee for eighteen months. Eighteen months before the onset of the pain she had fallen and was said to have fractured the neck of the right femur. She was able to move about with crutches after seven weeks and without them after twelve weeks. The pain in the right hip was noted first in walking. It grew worse until she walked with a marked limp and needed the support of a cane. She entered St. Luke's Hospital with the diagnosis of aseptic necrosis of the head of the right femur and hypertrophic arthritis of the peripheral portion of the hip joint. Dr. E. W. Ryerson removed the head of the right femur (fig. 7 *A* and 7 *B*) on Oct. 25, 1934. The almost hemispherical piece of bone was 5.5 by 4.8 cm. across the broken surfaces. The maximum thickness eccentrically was 2.6 cm. The fovea, 2 by 1.5 cm., was in

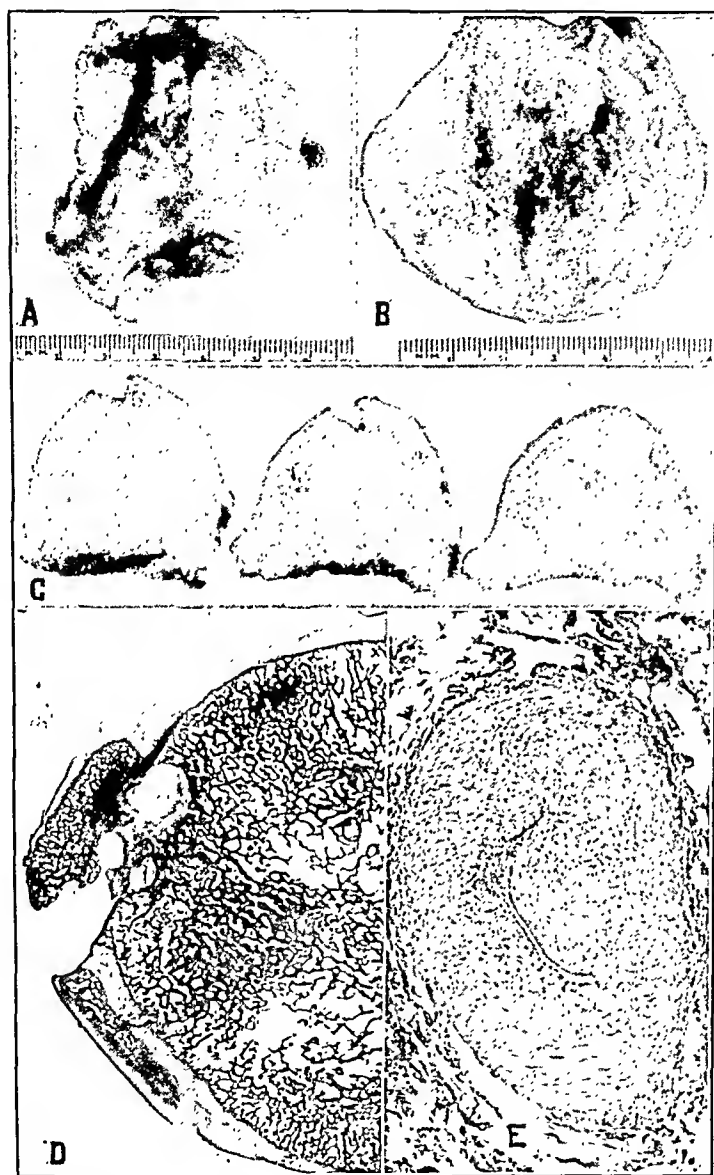


Fig. 6.—*A*, photograph illustrating the roughening of the articular surface of the head of the femur. Note the lip of bone tissue extending from the margin of the fovea (case 7). *B*, photograph of the bone surface made by amputating the head of the femur (case 7). *C*, surfaces made by sawing the head of the femur in front of the fovea, through the fovea and behind the fovea. Note the increased density of the spongiosa and the crevices filled with edematous fibrous tissue (case 7). *D*, photomicrograph of a section through the fovea, illustrating the changes in the bone structure (case 7). *E*, photomicrograph illustrating the fibrous tissue thickening of the intima and reduction in the lumen of nutrient arteries in the ligamentum teres (case 7).

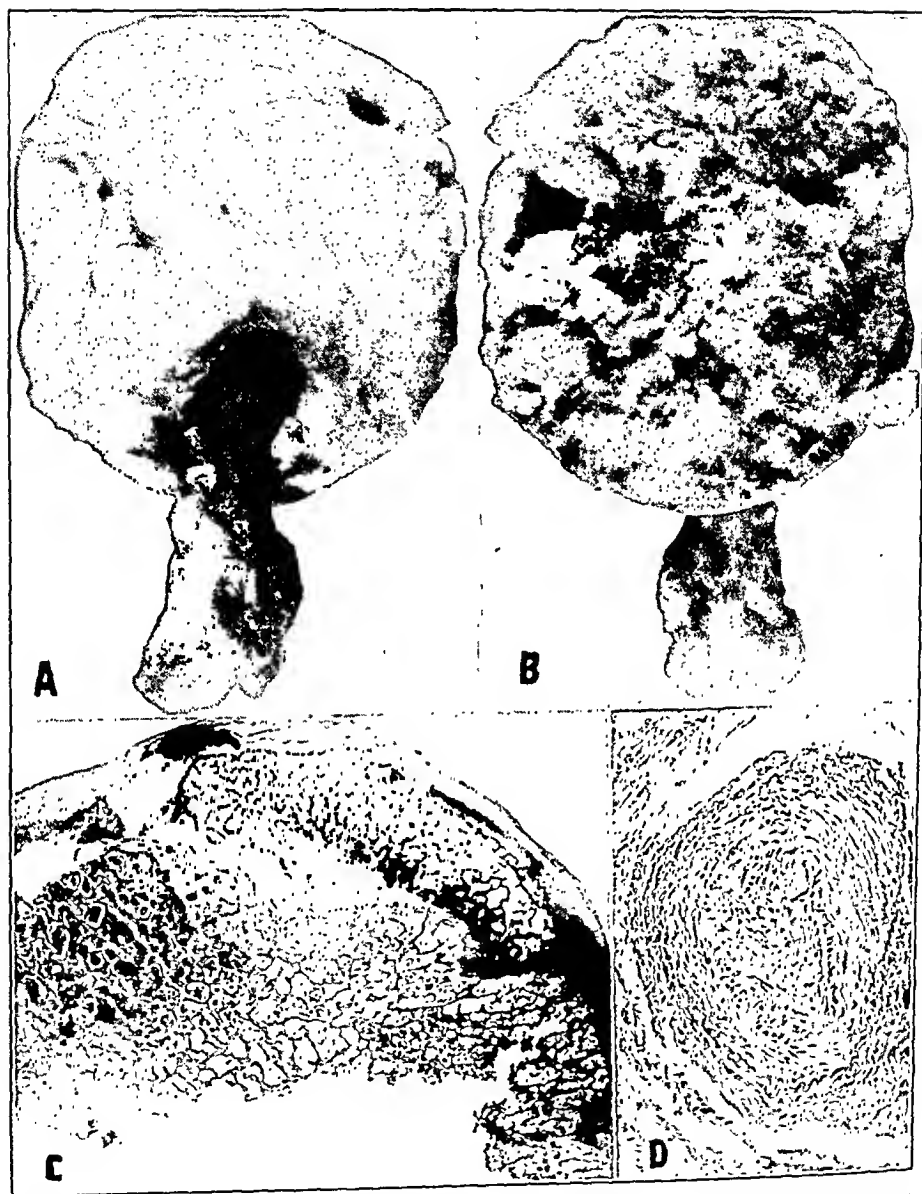


Fig. 7.—*A*, photograph of the amputated head of the femur with the attached ligamentum teres. Note the uneven articular surface (case 8). *B*, photograph of the surface made by amputating the head of the femur. Note the crevices and growths of fibrous tissues in the bone (case 8). *C*, photomicrograph of a section through the fovea. To the left in the illustration is a crevice. The articular cartilage has some attached necrotic bone. Beneath the crevice are other necrotic bone tissues and marrow spaces with "bone dust." On the right side of the illustration is a plate of restored bone, beneath which are other necrotic tissue (case 8). *D*, photomicrograph illustrating the fibrous tissue thickening of the intima and the reduced lumens of nutrient arteries in the ligamentum teres (case 8).

this portion of the articular surface. The ligamentum teres tissue attached to the fovea was 3.5 cm. long. At the fovea this edematous fibrous fat tissue was 8 mm. in diameter, at the other end 12 by 16 mm. The bone tissue in the surface made by amputating the femoral head was interrupted by several edematous bands of fibrous tissue 2 to 3 mm. wide, extending from the margins toward the center, more on one side than on the other. The bone tissue was sclerosed spongiosa. The surface of the articular cartilage was wrinkled. Several places were indented, and at least a half was loosely attached to the underlying bone. About a dozen irregular pieces of cortical and cancellous bone, some with wrinkled articular cartilage, formed a mass 5 by 4 by 3 cm.

Histologic preparations of a segment of bone 6 mm. thick cut from the center of the head through the fovea were prepared. The articular cartilage, with some bone, was detached from the margin to near the fovea, leaving a crevice (fig. 7C). The spongiosa beneath the crevice to the surface made by amputation was necrotic. The marrow spaces contained granular tissue *débris* and small fragments of necrotic trabeculae (bone dust). Beneath the fovea and extending to the opposite edge was a layer of bone 5 mm. thick, to which the articular cartilage was adherent. Beneath this layer of bone was a zone of compact and edematous fibrous tissue 5 mm. wide. This decreased in amount on both sides in the planes examined and toward the neck of the femur extended into necrotic bone. Many of the marrow spaces between this layer and the plane of the amputation contained granular tissue *débris*. There was no bone callus tissue except around the plate of bone directly beneath the fovea. The deeper portions of this plate were dense like cortical bone. The tissue of the ligamentum teres was sectioned for histologic examination at four levels, according to a sketch. In these levels the central portions were dense fibrous tissue; the peripheral portions were edematous connective tissue. Many arterial branches (fig. 7D) in this fibrous tissue had lumens reduced to small channels by concentric and eccentric fibrous tissue thickening of the intima.

CASE 9.—A white woman aged 33 had a constant ache or sharp pain in the left hip for twenty-one years. At the age of 15 years she had noticed a slight limp, which increased with her first pregnancy, at the age of 23. During childbirth and for two or three weeks thereafter the left hip was painful. With each of the succeeding three pregnancies the pain recurred, and after the last, at the age of 27 years, it became persistent. Six months before her admission to St. Luke's Hospital the pain became severe, and she walked with a noticeable limp. Dr. E. W. Ryerson on March 15, 1932, exposed the left hip joint and found a flattened femoral head with a thin piece of loosened articular cartilage and bone about 2.5 cm. in diameter on the superior surface. Bone tissue to a depth of about 2 cm. was removed. The diameter of the head was 6.5 cm. Near the center of the roughened articular surface was a rectangular piece of cartilage and bone 3.7 by 2.5 cm. by 6 mm. thick, hinged along one edge, raised slightly and loosely adherent to the bone tissues beneath. The surface made by the amputation was finely and coarsely porous sclerosed spongiosa. An irregular pocket near the center of this surface, 2.5 by 1 cm., contained loosely adherent, edematous connective tissue. The lining surfaces of the crevice were smooth sclerosed bone. The adjacent spongiosa also was dense. Tissues of the ligamentum teres were not submitted for histologic examination.

The hyaline articular cartilage was directly continuous with broad and narrow compact bone trabeculae. The large crevice in the bone extended at one place to near the articular cartilage. The lining of the crevice was a thin plate of compact

bone. The crevice was filled with edematous fibrillar connective tissue in which were a few medium-sized and small branches of nutrient arteries with narrow lumens. Concentric layers of coarse connective tissue fibers encircled these arteries (fig. 8 *A*), and outer portions of the walls of some of the larger showed fibrinoid degeneration. One of the latter was reduced to only a few smooth muscle cells

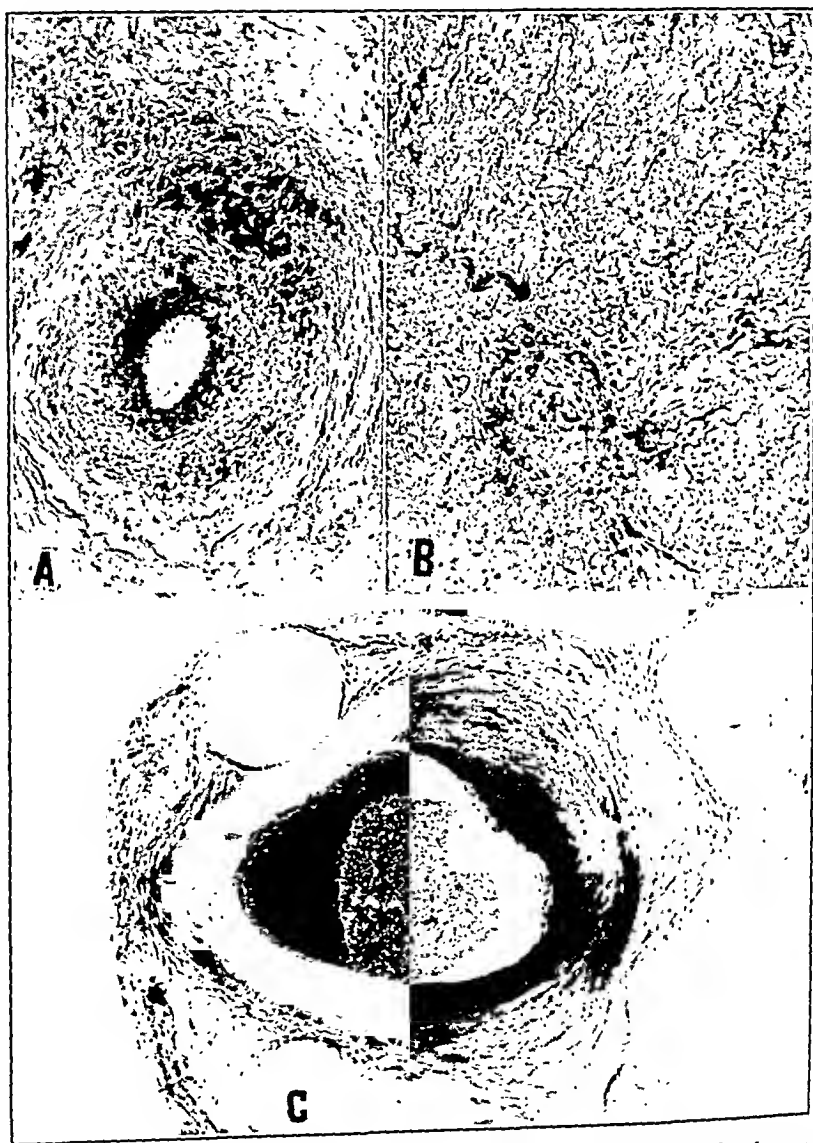


Fig. 8.—*A*, photomicrograph, $\times 105$, illustrating the wall of a blood vessel in the edematous connective tissue of the bone crevice. Note the fibrous tissue thickening of the wall and the edema of the supporting stroma (case 9). *B*, photomicrograph, $\times 105$, illustrating the edematous connective tissues in the bone crevice and the remaining structures of an arterial branch. Only a small capillary-like lumen remains (case 9). *C*, photomicrograph, $\times 105$, illustrating a large branch of a nutrient artery in the femoral head. The wall is thickened by fibrous tissue, especially along the intima. The lumen contains a mass of erythrocytes and leukocytes (case 10).

embedded in fibrous tissue and having a capillary-like lumen (fig. 8B). Small, narrow spaces immediately adjacent to the crevice contained mixtures of edematous fibrous and fatty tissues and small exudations of lymphocytes and plasma cells.

CASE 10.—A white man aged 64 was admitted to St. Luke's Hospital on Jan. 3, 1938, to the service of Dr. E. W. Ryerson, because of pain in the left hip for two years. About seven years before admission he fell from a ladder and fractured the proximal third of the neck of the left femur. The fracture seemed to have healed in about six months, with excellent restoration of function. The patient had pushed a cart on the streets until about four months before entering the hospital. Then the pain in the left hip had become marked, and he had a sensation of looseness in the joint. Roentgenograms disclosed flattening of the head of the femur and an increase of the angle caused by the old fracture of the femoral neck. Portions of the bone tissue were rarefied; other portions had increased density.

On January 6 Dr. E. W. Ryerson removed the head and portions of the neck of the left femur. The cone-shaped capital segment was 3.2 cm. thick, and the surface made by amputation was 6 by 5.5 cm. The fovea, lying eccentrically in the apex, was 2 by 1.5 cm. Edematous fibrous tissues of the ligament, 1.5 by 1.3 by 0.3 cm., were attached. The articular cartilage surfaces were uneven, and portions were loosened from the bone beneath. In some places the bone reached to the surface. The surface made by amputation contained broken cancellous bone tissue, some portions hyperemic, others yellow with fat. There were nine other pieces of bone, some from the head and others from the neck of the femur. The largest, with a convexly curved cartilage surface, was 5.5 by 2.5 by 2.5 cm. A crevice 2 by 1 cm. in the broken bone surface was filled with fibrous tissue.

A piece of bone 5 mm. wide was cut from the head of the femur in a plane through the fovea. Beneath the hyaline articular cartilage was a crevice filled with bone detritus and granular material. The bone tissues adherent to the cartilage had broad and narrow trabeculae. The marrow spaces near the cartilage contained fibrous tissue or fibrous and fatty tissue. Toward the crevice some of the fibrous tissue was necrotic. The edematous fibrous tissue attached to the fovea had nutrient arteries with muscular hypertrophy and fibrous thickenings of their walls. The lumens were narrow. The divisions of these vessels had small channels. A large nutrient artery deep in the bone (fig. 8C) had a thick fibrous wall, and along the lining was a mural mass of red blood cells and fibrin.

COMMENT

Constriction and occlusion of nutrient arteries or of their intrinsic divisions by fibroblastic tissue have an important causal relation to aseptic necrosis of bone. In many of the cases herein described the constriction or occlusion was the result of trauma. Whether the narrowed channels and the fibrous tissue-thickened arterial walls are the loci of the injury or represent changes following an occlusion more proximal in the artery cannot be determined from the histologic preparations. Such vascular lesions, however, affect the nutrition of the bone tissues into which the vessels originally extended.

The extent of bone infarction caused by traumatic occlusion of the nutrient arteries or of their intrinsic branches is determined by the amount of vascular damage. The subsequent fate of the necrotic bone

depends on the vascular restitution which follows. When this is adequate and when reparative tissues develop sufficiently to withstand the stress applied to bone tissue, permanent restoration of function occurs. Should the restitution be inadequate, the disability becomes chronic. If restitution is only temporarily sufficient, an interval of restored function merges gradually into disability with roentgenographic evidence of aseptic necrosis. Such progressive manifestations result from the initial vascular injury or from compression of the intrinsic branches of nutrient arteries when bone structures weakened by vascular disturbances collapse under stress.

Large regions of aseptic necrosis (infarction) in bone are usually recognized without difficulty in the roentgenogram. Small infarcts of bone may develop into an insidious disability, difficult to diagnose clinically. In case 5 a slight trauma had injured an important nutrient artery of the femoral shaft. The results of the localized infarct and the subsequent tissue reactions produced shadows in the roentgenograms, which were interpreted in various ways. When dislocations of small bones, such as the bones of the wrist, injure the nutrient arteries, functional restoration is complicated. Simple reduction, then, does not correct the disablement caused by aseptic necrosis of bone.

The intrinsic branches of nutrient arteries of bones have muscular walls and a tissue structure similar to that of arterial branches elsewhere. The conditions of vascular repair and tissue restoration in bone with aseptic necrosis (infarction) differ from those for soft tissues. In bone, revascularization of necrotic portions occurs through the intrinsic blood vessels rather than from arterial branches of the surrounding soft tissues. The strength of the regenerated bone in the healing process must suffice to protect the intrinsic arterial branches against further injury by compression. The regions of bone tissue commonly involved in aseptic necrosis are so located that almost complete restitution of form and structure is necessary to prevent a disablement caused by a contraction deformity of the tissues. In this respect, the healing of an infarct of the bone contrasts with that of similar lesions of soft tissues, in which contraction and absorption in the healing are compensated.

If systemic chemical changes of bone are fundamental in aseptic necrosis, as argued by Block, and the vascular lesions incidental, the lesions of aseptic necrosis should be multiple. On the contrary, multiple lesions are unusual except in cases in which the same trauma injures the circulation in more than one bone, for example, in both femurs. The extensive aseptic necrosis of bone observed in caisson disease, recently described by Phemister,¹¹ is caused by interruption of the nutrition (circulation) in the affected portions of bones by gases liberated in the tissues.

11. Phemister, D. B.: *Proc. Inst. Med. Chicago* 12:82, 1938.

SUMMARY

Aseptic necrosis, a localized nutritional disturbance of bone, is regarded by some as an infarct of the tissues. The association of arterial occlusions or constrictions with regions of aseptic necrosis has been suggested but not clearly demonstrated.

Thickening of the walls of nutrient arteries and of their intrinsic branches by fibroplastic tissue, markedly reducing the lumens, was associated with aseptic necrosis in 9 large and small bones. In 1 small bone (of the wrist) an obturating thrombus filled the channel of an arterial branch at the margin of the necrotic portion.

Probably the greater number of such vascular constrictions or occlusions are due to trauma. Whether the lesions observed are at the actual site of injury or represent changes secondary to a constriction more proximal in the arterial system has not been established.

The conclusion is reasonable that vascular constrictions such as have been described cause definite nutritional disturbances (infarction) of the bone into which the vessels extend.

ADHERENT POSTERIOR DUODENAL ULCER

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NEW YORK

In discussing the treatment of peptic ulcer, whether one is considering the medical or the surgical aspect of the problem one is confronted with the question of the treatment of duodenal ulcer, as approximately 85 per cent of all peptic ulcers are duodenal. Among 864 peptic ulcers which have come under observation during the past ten years in the gastroenterologic clinic of the fourth medical and surgical divisions of Bellevue Hospital, 88 per cent duodenal lesions have been encountered. The duodenal ulcer presents the chief problem both for the gastroenterologist and for the surgeon. It has been the policy in the clinic never to refer a patient for operation if any method of medical management would relieve the symptoms from which he was suffering. Therefore, during the past ten years only 10 per cent of the patients have been referred for operation. This point is important when one considers the pathologic process encountered in the late stages of duodenal ulcer and the type of operation essential to relieve the patient of his symptoms.

During the ten year period the 864 patients have made 16,776 visits to the clinic, an average of nineteen visits per patient. My impressions have been gained from personal observation of the patients in this clinic, as I have been in constant attendance during the entire period. Duodenal ulcer of fairly short duration (a year or less) offers a favorable prognosis if dietary management and general medical supervision are employed. From my observation it seems that 85 to 90 per cent of duodenal ulcers treated in the early stages can be cured or kept from producing symptoms with a medical regimen. When there is a history of symptoms of a number of years' duration the prognosis is definitely altered, bearing an inverse ratio to the number of years that the patient has been ill.

In this presentation I shall discuss the 10 per cent of duodenal ulcers for which operation was performed and the associated pathologic processes that were encountered. I shall also describe the treatment I consider necessary to restore the patient to health. When the gastroenterologic clinic was first organized (in January 1928) the chief objective was to determine whether any method of medical treatment would

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cure a duodenal ulcer. It was desired also to learn whether patients who could not be relieved by medical management could be permanently cured by any type of conservative gastric surgical operation. For the patients who were referred for operation during the first four years after the establishment of the clinic the operation performed was gastroenterostomy. After a few years enthusiasm for this procedure waned, as the patients on whom gastroenterostomy was performed had innumerable complaints. In 1933, Church and I¹ found that only 37 per cent of such patients were free from symptoms and that 16.4 per cent had marginal ulcers. In selected cases subtotal resection was done for duodenal lesions in 1932, and a posterior ulcer associated with an inflammatory process involving the head of the pancreas or the duodeno-hepatic ligament was a common finding. Since 1933 I have done subtotal resections exclusively for patients suffering from duodenal ulcer. It is this type of lesion that will be discussed at this time.

During the past four years and nine months, from Jan. 1, 1933, to Oct. 1, 1937, I have operated on 64 patients with duodenal ulcer. Thirty-two of the patients were referred from the clinic for persons with gastric disease of the Fourth Division at Bellevue Hospital, and 32 from my office.

It is essential to classify patients with duodenal ulcer into those on whom gastric operations have been previously performed and those on whom no such operation has been done. Of the 64 patients, previous gastric operations had been performed on 16, or 25 per cent. It is worth pointing out that these 16 patients had undergone twenty-four gastric operations before submitting to subtotal resection. Intractable pain furnished the reason for the radical operation, and 6 of the patients, in 10 instances, were operated on for multiple massive hemorrhages which were uncontrollable by medical management. The mortality in this group will be discussed later.

For the remaining 48 patients with duodenal ulcer primary subtotal resection was performed. This does not mean that laparotomy had never been performed on these patients; appendectomy or cholecystectomy had been performed on 13, or 27 per cent, and on several more than one exploratory laparotomy had been performed. For each of 3 patients three exploratory laparotomies had been done but had failed to disclose the cause of pain. It is the associated pathologic process encountered in the cases of these 48 patients that constitutes the chief interest in this presentation. Twenty-six, or 54 per cent, of these 48 patients had a posterior ulcer and definite chronic pancreatitis; in some

1. Church, R. E., and Hinton, J. W.: A Study of Six Hundred and Seventy-One Cases of Peptic Ulcer with Special Emphasis on One Hundred and Fourteen Postoperated Cases, *New York State J. Med.* **34**:1079 (Dec. 15) 1934.

cases the head of the pancreas was the size of a small orange, and in numerous instances it was the size of a lemon. Frequently the duodenohepatic ligament was also involved in the inflammatory mass. The associated pathologic process was unmistakable in every instance. Such single posterior ulcers do not represent the most extensive pathologic processes; it is with double duodenal lesions that the most marked pancreatitis is encountered, and each of 10, or 21 per cent, of the 48 patients had two ulcers in the duodenum. It is in such cases that one is liable to overlook the existence of pancreatic infection. The ulcer on the anterior surface of the duodenum gives one the impression that the lesion is only an anterior ulcer, but when patients with such a condition are operated on one is amazed at the extensive inflammatory involvement of the pancreas and the duodenohepatic ligament with a large posterior ulcer. The anterior ulcer usually proves to be relatively small. Deformity of the duodenum results from puckering caused by contracture of the scar tissue in and around the head of the pancreas.

This leaves among the 48 patients 12, or 25 per cent, who had an anterior ulcer which was penetrating or was adherent to the under surface of the liver or the gallbladder but no evidence of associated pancreatitis or involvement of the duodenohepatic ligament. If the patients with double ulcer are grouped with those with posterior ulcer it will be seen that 75 per cent of the patients in this series had a definite inflammatory process of the pancreas.

These patients were operated on for relief of either pain or hemorrhage; of the 48 patients, 39, or 81 per cent, were operated on for pain, and 9, or 19 per cent, were operated on for multiple massive hemorrhages that could not be controlled by medical management.

The clinical problem encountered for patients with chronic ulcer is to determine the stage at which the ulcer becomes adherent to an adjacent viscus. When this occurs the condition ceases to be amenable to medical management and requires immediate surgical intervention. Unfortunately there is no criterion for such a diagnosis except the history of pain and clinical judgment. The patient with a posterior ulcer and associated pancreatitis has a changed pain syndrome. The pain may be severe and may be referred to the back, either to the right or to the left of the spinal column. It may be so severe as to be confused with that caused by a renal calculus or by cholelithiasis. Of course, one always has the history of the previous symptoms of ulcer, and this is an invaluable aid in making a differential diagnosis. Unfortunately the gastrointestinal roentgenographic series is usually of little help in deciding whether a duodenal ulcer should be operated on. The findings may be indefinite, and if the lesion is a posterior ulcer the roentgenologist may be able to report only a duodenal deformity. Therefore, one should not be misled by the fact that the roentgenologist does not

give definite information. Pyloric obstruction may result from double duodenal ulcers of long standing, and occasionally it will result from a posterior ulcer. In only 15 per cent of my cases was there a definite organic obstruction of the pylorus.

Jones² in an article presented before the American Gastro-Enterological Association in 1936, on "The Surgical Aspect of Diseases of the Pancreas" stated: "I myself have never seen a case of chronic interstitial pancreatitis without hemorrhage or a fat necrosis diagnosed before operation. Such conditions have no symptoms as far as I can determine." I am forced to take issue with this statement. I feel that if one sees duodenal ulcers in the late stages of the disease one will definitely be able to make a clinical diagnosis of the associated pancreatitis and refer the patient for operation. The 48 primary ulcers operated on in this series had an average duration of symptoms of thirteen and nine-tenths years before operation. This delay was important in producing chronic pancreatitis.

None of the laboratory tests that I have had occasion to use are of any practical significance. I have used the amylase test of Elman and his associates³ on human beings and also on dogs in which the pancreatic ducts had been ligated, but I found that it gave no aid in diagnosing a chronic infection of the pancreas. The blood sugar curve is likewise of no value. Therefore, the diagnosis rests on the changed pain syndrome and the radiation of the pain to the back, with such severity that morphine or some other sedative is required to give relief.

For the past four years and nine months, as has been stated, for all duodenal ulcers on which I have operated the procedure has been subtotal resection. The operations included 16 secondary operations and 48 primary operations. In any discussion of resection for adherent posterior duodenal ulcer it should be made clear that for all the patients operated on the ulcer was completely removed from the pancreas or the duodenohepatic ligament. This point should be strongly emphasized, as I have had occasion to follow a few cases in which operation had been performed by other surgeons. The stomach had been resected and the inflammatory mass left in situ. The results were only fair. The pain suffered by the patient was apparently caused not by the ulcer but by the associated infection of the adjacent organ; therefore, one would hardly expect the patient to become free from symptoms if the ulcer is left in situ. The one argument used for not removing such a lesion

2. Jones, D. F.: Surgical Aspects of Diseases of the Pancreas, *Am. J. Digest. Dis. & Nutrition* 3:686 (Nov.) 1936.

3. Elman, R.; Arneson, N., and Graham, E. A.: Value of Blood Amylase Estimations in the Diagnosis of Pancreatic Disease, *Arch. Surg.* 19:943 (Dec.) 1929.

is the difficulty of freeing the ulcer and the high mortality associated with resection. For that reason the mortality in this series will be presented. For the 48 primary subtotal resections there were 2 deaths, or a mortality of 4.1 per cent. For the 16 secondary gastric operations there were 5 deaths, or a mortality of 31 per cent. In the entire series of 64 cases there were 7 deaths, or a total mortality of 10.9 per cent. The mortality among the patients on whom secondary operations were performed certainly should not be counted as part of the mortality entailed by subtotal resection, as in such cases one is forced to undo what another surgeon has done. It is doubtful whether the mortality for conservative operations for the nation at large is as low as the mortality for subtotal resection in cases of duodenal ulcer; the reason for this is that pyloroplasty and gastroenterostomy are rather frequently done, whereas resection is performed by comparatively few surgeons.

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SACROCOCCYGEAL TERATOMA IN THE ADULT

REPORT OF A CASE

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Teratomas, while no longer looked on as a judgment from God, continue to intrigue and mystify the student of oncology. As a group, teratomas are among the rare forms of growth. In previous communications by Hundling,¹ Moersch² and Whittaker and Pemberton,³ the rarity of sacral growths has been emphasized. These authors reported a total of 14 dermoids and 1 teratoma of the sacrococcygeal region. Whittaker and Pemberton concluded that ventral tumors of the sacrum occurred about once among 40,000 registrations at the Mayo Clinic and that only a small percentage of such tumors belonged to the group of congenital abnormalities. The rarity of teratoma of the sacrococcygeal region of adults, therefore, justifies this report. According to Harrington,⁴ the sites of occurrence of teratoma, in order of frequency, are the pelvis, the abdomen, the sacrococcygeal region and the thorax. To these should be added the nervous system.

The exact origin of teratoma has not been fully established. Much progress has been made in the understanding of teratoma since Baillie's⁵ report, in 1789, of an ovarian teratoma which occurred in a virgin girl aged 11. This was a severe blow to the prevalent idea that such tumors were the result of immoral practices. One must, however, content oneself with various hypotheses as to their origin. These have been clearly stated by Marshall,⁶ who closely followed the work

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1. Hundling, H. W.: Ventral Tumors of the Sacrum, Surg., Gynec. & Obst. **38**:518-533 (April) 1924.

2. Moersch, F. P.: Sacral Tumors: Report of Forty-Two Cases with Special Reference to Their Neurologic Aspects, M. Clin. North America **10**:715-727 (Nov.) 1926.

3. Whittaker, L. D., and Pemberton, J. deJ.: Tumors Ventral to the Sacrum, Ann. Surg. **107**:96-106 (Jan.) 1938.

4. Harrington, S. W.: Surgical Treatment in Eleven Cases of Mediastinal and Intrathoracic Teratomas, J. Thoracic Surg. **3**:50-72 (Oct.) 1933.

5. Baillie, cited by Marshall.⁶

6. Marshall, G. G.: Dermoid Teeth in External Auditory Canal, with Comments on Teratomas and Dermoids in General, New England J. Med. **214**:202-204 (Jan. 30) 1936.

of Ewing.⁷ They are: (1) defective closure of clefts with cellular inclusions; (2) misplaced blastomeres; (3) wandering of germ cells in the development of the embryo, and (4) parthenogenesis. Ewing classified these new growths as follows: monsters, teratomas, teratoid tumors, mixed tumors, dermoids and epidermoids. Briefly, it may be said that a teratoma is considered to be derived from all three germ layers, in contradistinction to a dermoid, which is derived from the ectodermal germ layer. Teratomas and dermoids are composed of both mature and embryonic cells. The latter cells tend to become malignant. Because of the uncertainty of differentiation of these various growths, Harrington has gone so far as to suggest that all such tumors be classified under the general heading of teratoma.

In a consideration of teratoma of the sacrococcygeal region, it has been well stated that the caudal end of the embryo represents a "Sargasso sea and the growths arising there produce a veritable potpourri of fetal tissues." The more important embryonal structures which give rise to sacrococcygeal growths are the coccygeal vestiges, the neur-enteric canal, the postanal gut and the proctodeum. The more common abnormalities resulting from congenital embryonal disorders in the sacrococcygeal region are the teratoid tumors (teratomas and dermoids). The subject of chordoma, a tumor which is also of embryonal origin, has been fully reviewed by Fletcher, Woltman and Adson;⁸ this tumor is not to be considered under the heading of teratoma. As a rule, teratoma of the sacrococcygeal region is not associated with neurologic changes, but at times defects of the spinal column and of the spinal cord and its membranes may occur. It should be stated in passing that teratoma of the spinal cord itself is rare, but cases which have been reported by Bucy and Buchanan,⁹ Kubie and Fulton¹⁰ and others indicate that any part of the spinal cord may be the site of a teratoma.

Teratoma of the sacral or sacrococcygeal region is probably present at birth and, according to Ewing, may be on the dorsal or the anterior side of the sacrum or the coccyx. Hansmann and Berne¹¹ were of the opinion that such a growth always originates retrorectally and that it

7. Ewing, J.: *Neoplastic Diseases*, ed. 3, Philadelphia, W. B. Saunders Company, 1928, pp. 1016-1037.

8. Fletcher, E. M.; Woltman, H. W., and Adson, A. W.: *Sacrococcygeal Chordomas: A Clinical and Pathologic Study*, *Arch. Neurol. & Psychiat.* **33**: 283-299 (Feb.) 1935.

9. Bucy, P. C., and Buchanan, D. N.: *Teratoma of the Spinal Cord*, *Surg., Gynec. & Obst.* **60**:1137-1144 (June) 1935.

10. Kubie, L. S., and Fulton, J. F.: *A Clinical and Pathological Study of Two Teratomatous Cysts of the Spinal Cord, Containing Mucus and Ciliated Cells*, *Surg., Gynec. & Obst.* **47**:297-311 (Sept.) 1928.

11. Hansmann, G. H., and Berne, C. J.: *Sacrococcygeal Teratomas*, *Arch. Surg.* **25**:1090-1097 (Dec.) 1932.

gradually may force its way to the posterior part of the sacrum. Bucy and Haymond,¹² in a review of the literature on teratoma since 1800, said that teratoma of the dorsal part of the sacrum is rare in comparison with teratoma of the anterior part of the sacrum. A growth on the dorsal aspect of the sacrum may be associated with an anomaly of the neural canal, while one of the anterior portion of the sacrum is said to have no connection with the spinal cord or its membranes.

While sacrococcygeal teratoma is not common, it is of sufficient frequency to warrant consideration in the presence of a tumor of this region. Hansmann and Berne in 1932 reported a group of 26 cases of sacrococcygeal teratoma; 25 were collected from the literature between the years 1924 and 1929, and he added 1 case which he had observed personally. In these 26 cases, 19 of the patients were females and 6 were males; in 1 case the sex was not stated. Hosoi¹³ in a review of cases of teratoma of the brain found that the incidence according to sex was reversed. In the majority of cases reported in the literature the teratoma occurred in a newborn or in a young infant. All of Hansmann's and Berne's 26 patients were less than 21 months of age. Love and Kernohan¹⁴ have shown that in cases of dermoid tumor of the central nervous system the average age at the time of operation is 23 years. This is in contradistinction to the age incidence of teratoma. Kubie and Fulton reported a case of teratoma of the cervical segment of the spinal cord in which the patient was 27 years of age. As far as we have been able to determine from a review of the literature, there are relatively few reports of teratoma of the sacrococcygeal region of the adult. The reason for this is that the presence of the growth is discovered soon after birth. The patient is operated on and the growth removed, or the patient succumbs to the growth or to an unsuccessful operation before he reaches adult life. Nicholson¹⁵ in 1937 reported a sacrococcygeal teratoma which contained three metatarsal bones and digits; the patient was a Chinese girl aged 16. Brines¹⁶ in 1934 reported

12. Bucy, P. C., and Haymond, H. E.: Lumbosacral Teratoma Associated with Spina Bifida Occulta: Report of a Case with Review of the Literature, *Am. J. Path.* **8**:339-345 (May) 1932.

13. Hosoi, K.: Teratoma and Teratoid Tumors of the Brain. *Arch. Path.* **9**:1207-1219 (June) 1930; Intradural Teratoid Tumors of the Spinal Cord: Report of a Case, *ibid.* **11**:875-883 (June) 1931.

14. Love, J. G., and Kernohan, J. W.: Dermoid and Epidermoid Tumors (Cholesteatomas) of the Central Nervous System, *J. A. M. A.* **107**:1876-1882 (Dec. 5) 1936.

15. Nicholson, G. W.: Studies on Tumor Formation: A Sacrococcygeal Teratoma with Three Metacarpal Bones and Digits, *Guy's Hosp. Rep.* **87**:46-106 (Jan.) 1937.

16. Brines, R. J.: A Large Teratoma Containing Rudimentary Arm Bones and a Hand, *J. A. M. A.* **103**:338 (Aug. 4) 1934.

a case similar to ours, that is, a case in which a large teratoma contained rudimentary arm bones and a hand; the patient was a man aged 24. The tumor weighed 31 pounds (14.1 Kg.) and was attached to one side of the coccyx. It was removed successfully, and the patient's convalescence was uneventful. Aloï¹⁷ reported a case in which a girl aged 19 had a teratoma of the lumbosacral region; the tumor was associated with spina bifida, but there was no involvement of the central nervous system. Bucy and Haymond and also Sonntag¹⁸ have reported 2 similar cases, in which the patients were children. It may be doubted that such lumbosacral teratomas should be included under the general heading of sacrococcygeal teratoma. They are referred to here because no region of the spinal column appears to be exempt from such embryologic abnormalities.



Fig. 1.—Tumor of the right buttock.

REPORT OF CASE

A man aged 21 was admitted to the clinic in April 1936, because of a cystic tumor of the lower end of the spinal column, which had been present since birth. There was no history of disturbance of the function of the lower extremities or of the bowel or the bladder. The growth had gradually enlarged since birth and had kept pace with the general development of the patient. The tumor had never caused much trouble unless injured. At one time, after the patient had ridden on a farm machine over rough ground, the mass had become so tender and swollen that he had had to remain in bed for several days.

The family history revealed that the father had had a tumor on his back, but the nature of the tumor was unknown. The patient had five brothers and

17. Aloï, V., cited by Bucy and Haymond.¹²

18. Sonntag, F.: Angeborener Misch tumor der Lendenkreuzbeingegegend nebst Spina bifida occulta, München. med. Wchnschr. 72:516-517 (March 27) 1925.



Fig. 2.—Specimen removed at operation. At the top of the photograph, on the left, can be seen the cut end of the bone of the forearm which was attached to the coccyx.

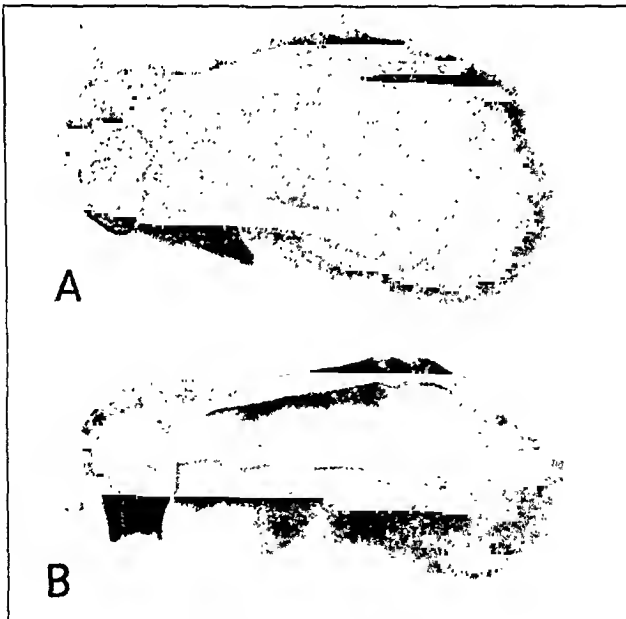


Fig. 3.—*A*, anteroposterior roentgenogram of the specimen, showing the bones of the hand. *B*, lateral roentgenogram of the specimen, showing the phalanges, the metacarpal bones, the carpal bones and the bone of the forearm which was resected from the coccyx.

three sisters, who were living and well when he came to the clinic. One brother had a harelip. There were no other developmental anomalies in the family.

Physical examination of the patient revealed no abnormality except a mass which was apparently attached to the end of the spinal column and extended out into the right buttock (fig. 1). The mass was not tender, and there were no signs of inflammation. On rectal examination the mass could be felt projecting toward the rectum on the right side. A careful neurologic investigation revealed no evidence of involvement of the central nervous system. The urine and the blood were normal. The flocculation test for syphilis gave a negative reaction. Roentgen examination of the sacrum disclosed a large cystic mass which was situated posterior to the lower part of the sacrum but apparently was not directly connected with it. Within the tumor mass one could distinguish well formed bony structures. The diagnosis was congenital tumor.

On April 14, 1936, the tumor (fig. 2) was removed by one of us (J. G. L.). The growth was situated at the lower end of the sacrum; it protruded into the right buttock, which was deformed, and extended across the midline, causing a deformity of the left buttock. The tumor was removed without any of the cysts being opened. It was attached by bone to the lower end of the coccyx on the right side. There was no connection with the meninges, and there was no suggestion of a meningocele. The tumor was intimately adherent to the rectum, and this structure had to be carefully dissected away from the tumor. This was done without injury to the bowel or to its blood supply. The tumor measured 10 by 5.5 by 33.5 cm. and weighed 117 Gm. When it was opened it was found to be cystic. It contained, in addition to the bones shown in the roentgenogram, hair and sebaceous material. The bones were well formed, and on the terminal phalanx of each finger was a long nail (fig. 3). The pathologic diagnosis, by Dr. J. W. Kernohan, was teratoma. The patient's convalescence was uneventful. When he was dismissed from the hospital, fourteen days after the operation, the results of neurologic examination were entirely negative, and his general condition was satisfactory. Recently (September 1937) a report from the patient's local surgeon stated that the patient had bruised his wound; this caused an abscess which had to be evacuated.

COMMENT

Sacrococcygeal tumors have been recognized for a long time, although their occurrence among adults is rare. A study of sacrococcygeal tumors reveals that they tend to be associated with the presence of rudimentary organs. Hosoi and others were inclined to agree that the origin of teratoma cannot be explained on the basis of a single embryologic maldevelopment as an invagination of the ectoderm at the time of closure of the primitive streak. On the contrary, this growth is derived from more than one germ layer and, as can usually be demonstrated, is trigeminal in origin.

The site of origin of sacrococcygeal teratoma is probably always retrorectal. The tumor may be attached to the rectum, to the sacrum or to the coccyx. Lumbosacral teratoma is closely related to sacrococcygeal teratoma but probably originates from a different embryonic focus. From a review of the literature it appears that the occurrence of teratoma has no relation to sex.

In the diagnosis of sacrococcygeal teratoma it must be recalled that if the tumor is situated anterior to the sacrum it may escape detection for many years. Consequently, in a case in which a sacral growth is suspected a careful rectal examination should be made in addition to the usual roentgenologic studies, as the latter may fail to reveal osseous changes. As reported by Fletcher, Woltman and Adson, chordoma is not infrequently present in the sacrococcygeal region and must be distinguished from teratoma. Other conditions to be considered in the differential diagnosis are tumor of the spinal cord, primary malignant tumor of the pelvis, metastatic growth, pelvic tumor (such as ovarian cyst), fibromyoma, adenoma, rectal fistula, pararectal abscess and finally spina bifida and meningocele.

De Veer and Browder¹⁹ have laid down the following six points to aid in distinguishing meningocele from teratoma: 1. The skin covering a teratoma is usually normal, while the skin covering a meningocele or a myelomeningocele is of embryonal type. 2. A teratoma is usually larger and extends into the pelvis, while a meningocele is smaller and rarely extends anterior to the sacrum. 3. A teratoma tends to grow more rapidly than does a meningomyelocele. 4. A teratoma is solid and as a rule is not connected with the spinal canal, while a meningocele tends to be softer and does contain spinal fluid. 5. In cases of teratoma there are rarely any neurologic complications; in cases of meningocele or meningomyelocele neurologic complications frequently occur. 6. Hydrocephalus is a frequent accompaniment to a meningocele or a meningomyelocele, but it never is associated with a teratoma.

Teratoma of the spinal column is not confined to the sacrococcygeal region. It has been found in the cervical, thoracic and lumbosacral segments of the spinal cord and in the sacrococcygeal region.

As has been well demonstrated by the case which we have reported and by other cases reported in the literature, surgical removal of a sacrococcygeal teratoma is always worthy of consideration, and unless there is involvement of the spinal cord the results are exceedingly satisfactory.

19. de Veer, J. A., and Browder, J.: Sacrococcygeal Teratoma, *Ann. Surg.* 105:408-417 (March) 1937.

STERILIZATION OF THE AIR IN THE OPERATING ROOM BY BACTERICIDAL RADIANT ENERGY

RESULTS IN OVER EIGHT HUNDRED OPERATIONS

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In previous publications¹ attention has been called to the prevalence of pathogenic bacteria, predominantly staphylococci, in the air in the operating room. Various precautions and procedures undertaken to eliminate these organisms from the air have been described. These preliminary measures were only partly effective, the most satisfactory being rigid isolation with reduction of the number of occupants to the minimum and forced ventilation with large quantities of air free of bacteria. The lowest bacterial contamination occurred during those periods when there were the fewest carriers among the operating room personnel and the general population. Since the number of carriers could not be controlled and since isolation and ventilation were only partly effective in freeing the air of bacteria, I turned to bactericidal radiant energy as a means of sterilizing the contaminated air in the region of the operative incision and the supply tables.² In continuation of work previously described¹ the bactericidal efficiency of these rays

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1. Hart, D.: Operation Room Infections: Control of Air-Borne Pathogenic Organisms, with Particular Reference to the Use of Special Bactericidal Radiant Energy; Preliminary Report, *Arch. Surg.* **34**:874-896 (May) 1937; Pathogenic Bacteria in the Air of Operating Rooms: Their Widespread Distribution and Methods of Control, *Arch. Surg.* **37**:521-530 (Oct.) 1938.

2. So-called sterile supply tables should never be left unprotected when this can be avoided. The table should be covered with a sterile sheet when it is not in use. While in use the table can be protected by general sterilization of the air, or, if there is objection to this, by an irradiation unit with a reflector which concentrates the rays on the table and prevents them from irradiating the entire room. With such a unit there is no necessity to cover all exposed cutaneous areas of the occupants of the room. However, any one who for a long time looks at the polished instruments, which might reflect a small amount of the radiation, should at least protect his eyes with glasses. If there is any tendency to cutaneous irritation from this small amount of reflected radiation it could probably be overcome by the application of cold cream to the skin before exposure.

has been reported³ and a statistical analysis of small numbers of cases given.⁴

This report gives a brief analysis of the results obtained in a total of 456 clean primary incisions and 86 reopened clean incisions out of over 800 operations performed in a field of bactericidal radiation.⁵ The other operations had a potential source of infection, and data on them were not used for the statistics. The operations in the present series were gastric or intestinal resections, cholecystectomies, appendectomies and amputations of gangrenous extremities. It is my impression that there has been a striking improvement in the postoperative course of these patients, but a statistical analysis was not made, since the results would

TABLE 1.—*Analysis of Clean Operative Incisions With Regard to Infections*

Service	Without Bactericidal Radiation			With Bactericidal Radiation		
	Total Cases No.	Infections		Total Cases No.	Infections	
		No.	Percentage		No.	Percentage
Urology.....	53	7	13.0	2	0	0
Orthopedies.....	144	5	3.5	65	0	0
Obstetrics and gynecology.....	245	7	3.0	1	0	0
General surgery.....	356	13	3.6	290	2*	0.7
Total.....	798	32	4.0	367	2*	0.5
Reopened clean incisions.....	65	25	38.5	80	3†	3.4
Incisions with potential source of infection.....	45	11	24.5	86	7‡	8.1

* Cases 1 and 2.

† Cases 3, 4 and 6.

‡ Cases 5, 7, 8, 9, 10, 11 and 12.

In the past year and a half, most of the operations of magnitude have been performed in a field of bactericidal irradiation. This group, therefore, is composed largely of the operations of this type which are known from experience to be most likely to be followed by infection. The group in which radiation was not used, on the other hand, contains a higher percentage of operations of lesser magnitude in which infections are less likely to occur.

have been difficult to evaluate. In general, I may say that unexplained infections in primary incisions have been almost, if not entirely, eliminated (table 1).

More striking than this reduction in the number of infections (either gross suppuration or demonstration of organisms in the wound) has

3. Hart, D.: Sterilization of the Air in the Operating Room by Special Bactericidal Radiant Energy, *J. Thoracic Surg.* 6:45-81 (Oct.) 1936.

4. Hart, D.: Sterilization of the Air in the Operating Room with Bactericidal Radiation: Comparative Analysis of One Hundred and Thirty-Two Stages of Extrapleural Thoracoplasties Performed with Radiation and One Hundred and Ten Stages Performed Without Radiation, *J. Thoracic Surg.* 7:525-535 (June) 1938.

5. This work has been made possible by the cooperation of the Westinghouse Electric and Manufacturing Company, which has supplied the radiation tubes and accessory electrical supplies. The statistical studies were made with the cooperation of Dr. Stokes Munroe and Dr. Phillip B. Parsons of the surgical staff.

been the reduction in the elevation of temperature following operation and the shortening of the duration of this postoperative elevation. Equally impressive has been the improvement in the postoperative course of the patients. They show less reaction in every way; there is less tenderness in the incision, and the period of convalescence is reduced.

In a consideration of the statistics, the summaries of all cases in which possible infection existed (cases 1 to 12 inclusive) should be carefully analyzed, note being taken of whether or not there is any doubt as to the presence of wound infection, the extent of the infection, the probable source of the contamination and the slight elevation of temperature in most cases.

In a number of cases, conditions classed as infections would have been overlooked except for careful observation and cultures of material from the wounds. Some of these conditions probably should not be classed as infections since the organisms were obtained only about the sutures which had been left in place for seven to nine days (cases 2 and 4) while in 1 case there was apparently inversion of the edge of the skin and organisms were cultured from the resultant granulating area (case 1). One should note whether the infection occurred in a primary incision or followed a second operation through a reopened incision. In the latter instance the organisms may have entered the subcutaneous tissues along the skin sutures of the preceding operation. In every primary incision showing any growth of organisms there was an evident source of the infection (cases 2, 3 and 6) or else there was doubt as to whether or not wound infection was present (cases 1 and 4). In all reopened wounds the skin sutures for the preceding operation formed a channel along which organisms could grow to gain access to the subcutaneous tissues. In 2 of the 7 reopened wounds which showed subsequent infection (cases 5, 7, 8, 9, 10, 11 and 12) there had been demonstrable infection about the skin sutures for the preceding stage of the operation (cases 4 and 6). In 1 the organism had been cultured from the skin sutures of the preceding stage but there was no evidence of wound infection (case 11). In another, in which there was no evidence of infection for the first two stages, a smear made during the third operation of material from the subcutaneous tissues at the level at which the skin sutures for the preceding stages had passed through showed an occasional coccus (case 12).

A statistical analysis of the 456 primary clean incisions, including the first stage of extrapleural thoracoplasties and 86 clean wounds that were reopened (extrapleural thoracoplasties for second and third stages), will be compared with the results obtained in similar groups of cases, in which the patients were operated on under the same conditions but

without the use of bactericidal radiant energy. The postoperative course of these two groups will be considered in the following order:

1. Number of infections (by services).
2. Infection and mortality statistics for extrapleural thoracoplasties, radical mastectomies and inguinal herniorrhaphies.
3. Postoperative elevation in temperature.
4. Duration of elevation in temperature following operation.
5. Wound healing and local reaction.
6. General systemic reaction.

For the group in which radiant energy was employed, a brief summary of each case classed as possibly presenting wound infection is given, together with the temperature curve for eight days after operation (cases 1 to 12, inclusive). It is not considered necessary or advisable to give abstracts and temperature curves for all the cases of infection in which bactericidal radiant energy was not used. The temperature, however, was much higher and the elevation was usually of longer duration than in the group for which irradiation was used. I recall (without a complete analysis of records) that over a period of several years, before the use of bactericidal radiation was begun, there were several deaths from infections with the hemolytic staphylococcus in supposedly clean operative wounds (3 craniotomies, 1 radical mastectomy, 4 extrapleural thoracoplasties⁶) and there were undoubtedly others. There has been no death from infection in cases in which the patients were operated on in a field of sterile air.

1. The number of infections has been greatly reduced (table 1). Considered by services, the orthopedic, the general surgical and the thoracic division are of greatest significance, since they have the largest number of cases. In the orthopedic service the infection percentage was reduced from 3.5 to 0. In the general surgical service while the reduction, as shown in table 1, was only from 3.6 to 0.7 per cent, a study of the summaries shows that in 1 case (case 1) it is extremely probable that the wound should not be classed as infected and that in the other (case 2) the only infection was an abscess about a single suture. Counting both of these cases as instances of infection, the percentage of infections in all cases, exclusive of cases in which thoracic operations were done, has been reduced from 4.0 to 0.5.

Thoracic operations are considered separately, since they are frequently multiple stage operations. In the series in which bactericidal radiant energy was not used, each operative procedure was carried out through a separate cutaneous incision because of fear of lighting up a dormant infection in the old incision. It is noteworthy that in this series in

6. Thoracoplasties performed without the use of bactericidal radiant energy are included in this statistical study.

which separate incisions were used there were 38.5 per cent infections in the first stage and only 24.5 per cent in the subsequent stages (tables 1 and 2). In the series in which bactericidal radiant energy was employed the wounds were reopened for the second and third stages. The only infections in primary incisions (3 cases, or 3.4 per cent; see tables 1 and 2) are readily explainable as follows: The report of case 3 shows that there was gross contamination of the wound with infected perspiration as the result of tearing of a glove; the report of case 4 shows that in this case the upper end of the incision was exposed by slipping of the dressing; there was maceration caused by the patient's lying on the suture line; the skin sutures were left in for nine days, and a positive growth of *Staphylococcus aureus* was obtained from moisture along the suture line. The wound was described as well healed three days after the sutures were removed. The report of case 5 shows that the patient had acne with a pustular eruption over the back, and the incision was made with the cutting current with the idea of avoiding smearing organisms from the infected hair follicles and glands through the wound. Poor healing was the result. The dressing slipped, exposing the incision, and subsequently there was superficial infection in this area. After the operations in which a preexisting wound (usually of two to four weeks' duration) has been reopened, 8 per cent of patients have shown some infection (tables 1 and 2).

In all cases the infection has been localized, and in most of them it has been mild (cases 5, 7, 8, 9, 10, 11 and 12). It is my opinion that in most, if not all, of these cases the organism present in the hair follicles and sweat glands grew along the silk skin sutures for the preceding operation, thus reaching the subcutaneous tissues, where they lay relatively dormant until stirred up and spread by the subsequent operative procedure. Physicians are familiar with the fact that when the skin sutures are left in place for an unduly long time, these organisms may cause small abscesses about the sutures. There are many advantages in operating through the same incision, and since all but one of the infections have been mild I am still following this technic, in the hope that even such infections can be eliminated. Recently I have closed a number of extrapleural thoracoplasty wounds with deep sutures of catgut and a subcuticular suture of wire. In no case in which the wound was so closed has any infection followed reopening of the incision, regardless of whether the wound was reclosed with catgut and wire or with catgut and skin sutures of silk. The wire is removed at the following operation but can be removed at any time without an anesthetic by exposure through a few small nicks in the freshly healed scar.

2. Infection and mortality statistics for extrapleural thoracoplasties, radical mastectomies and inguinal herniorrhaphies are considered sepa-

7. This includes all cases in which there was either gross suppuration or a positive growth of organisms from smears made from the suture line.

rately, since cases in which these procedures are used form the relatively large series. This also allows a comparison of the results following operations of greater magnitude, such as thoracoplasties and mastectomies, with the results following the smaller operative procedures, as represented by inguinal herniorrhaphies (table 2). Infections following thoracoplasties have been considered. It should be noted that the reduction in the mortality from extrapleural thoracoplasties has been brought about by elimination of the mortality from wound infection in the series in which bactericidal radiant energy was employed (table 2). There has been no death in the other two series either with or without the use of this measure. For radical mastectomies the infections⁸ have been cut from 31 to 2.6 per cent (a single stay suture abscess appearing on the eighth postoperative day in case 2) while for inguinal hernior-

TABLE 2.—*Infection and Mortality Statistics for Clean Operative Incisions*

Type of Operation	Without Bactericidal Radiation								With Bactericidal Radiation								
	Total Number of Cases	Wound Infection		Mortality from Wound Infection		Total Mortality		Total Number of Cases	Wound Infection		Mortality from Wound Infection		Total Mortality				
		No.	%	No.	%	No.	%		No.	%	No.	%	No.	%			
Thoracoplasty																	
First stage...	65	25	38.5	3	4.6	3.6	5	7.7	5.5	89	3*	3.4	0	0	2	2.2	2.0
Subsequent stages.....	45	11	24.5	1	2.2					86	7†	8.1	0	0	3	3.5	
Radical mastectomy.....	13	4	31.0	0	0	0	0			33	1‡	2.6	0	0	0	0	
Inguinal herniorrhaphy.....	150	5	3.3	0	0	0	0			87	1§	1.1	0	0	0	0	

* Cases 3, 4 and 6.

† Cases 5, 7, 8, 9, 10, 11 and 12.

‡ Case 2.

§ Case 1.

rhaphies the infections have been cut from 3.3 per cent probably to 0, or to 1.1 per cent if a case in which it is very doubtful that the wound was infected (case 1) is included. In this case it is probable that the edge of the skin was inverted and that the organisms were cultured from the resulting small area of granulation tissue.

3. The reduction in postoperative elevation of temperature has been most striking. I feel that this, together with the shorter duration of elevated temperature, the diminished reaction in the wound and the less severe systemic reaction of the patient, are as important as, if not more important than, the reduction in the small percentage of diagnosed infections. All are indications of the reduction in the amount of bacterial contamination of the wound. The dividing line between the mild and the more pronounced elevations in temperature is taken as 38 C., or 100.4 F. For those who care to go into a more detailed

8. Gross suppuration or positive culture from the wound.

analysis, the smaller temperature divisions, with the number and percentage of cases in each, are given in tables 3, 4 and 5. By the use of bactericidal radiation to sterilize the air the percentage of patients

TABLE 3.—*Extrapleural Thoracoplasty for Pulmonary Tuberculosis; Temperature Elevation (Centigrade)*

Before Operation					After Operation			
Without Radiation		With Radiation		Temperature Groups	Without Radiation		With Radiation	
No.	Percentage	No.	Percentage		No.	Percentage	No.	Percentage
97	88.2	152	87	37-36.5	2	2	37	21.0
12	10.8	20	11	37-38.0	33	30	85	49.0
1	1.0	3	2	37-39.0	58	52	46	26.0
0	0	0	0	37-40.0	16	15	6	3.5
0	0	0	0	37-41.0	1	1	1	0.5
Total.....					110	100	175	100

TABLE 4.—*Radical Mastectomy; Temperature Elevation (Centigrade)*

Before Operation					After Operation			
Without Radiation		With Radiation		Temperature Groups	Without Radiation		With Radiation	
No.	Percentage	No.	Percentage		No.	Percentage	No.	Percentage
12	92.3	37	97	37-37.5	0	0	1	3
1	7.7	1	3	37-38.0	7	53.8	24	63
0	0	0	0	37-39.0	5	38.5	13	34
0	0	0	0	37-40.0	1	7.7	0	0
0	0	0	0	37-41.0	0	0	0	0
Total.....					13	100	38	100

TABLE 5.—*Inguinal Herniorrhaphy; Temperature Elevation (Centigrade)*

Before Operation					After Operation			
Without Radiation		With Radiation		Temperature Groups	Without Radiation		With Radiation	
No.	Percentage	No.	Percentage		No.	Percentage	No.	Percentage
140	93.3	83	95.4	37-37.5	14	9.3	12	13.8
8	5.3	4	4.6	37-38.0	82	54.7	56	64.4
2	1.3	0	0	37-39.0	47	31.3	19	21.8
0	0	0	0	37-40.0	7	4.7	0	0
0	0	0	0	37-41.0	0	0	0	0
Total.....					150	100	87	100

having a temperature above 38 C. (100.4 F.) after operation was reduced as follows:

Thoracoplasties, from 68 to 30 per cent.

Radical mastectomies, from 46 to 34 per cent.

Inguinal herniorrhaphies, from 36 to 22 per cent.

4. With sterilization of the air in the operating room the shortening of the duration of elevated temperature following operation has been even more striking than the lowering of the temperature elevation (tables 6, 7 and 8). Taking four days as the dividing line between a relatively short and a more prolonged duration of elevated temperature, one finds that in cases in which bactericidal radiation was used the number of patients showing the longer course of fever has been reduced as follows:

Extrapleural thoracoplasties, from 78 to 22 per cent.

Radical mastectomies, from 54 to 21 per cent.

Inguinal herniorrhaphies, from 46 to 14 per cent.

For a more detailed analysis of the duration of high temperature the reader is referred to tables 6, 7 and 8.

5. By the use of bactericidal radiation, wound healing has been improved and the local reaction has been greatly diminished. The wounds usually remain dry, and there is little redness of the skin unless the patient lies on the incision (particularly in the summer, when there is much perspiration) or the sutures are left in place for an unduly long time (see report of case 4). The deep-seated reaction is diminished even when closure is made with catgut. The most striking difference noted is the diminution in the amount of soreness and pain in the incision. This is particularly evident in thoracoplasties.

6. The general systemic reaction of the patient after the operation is much less severe when the air is sterilized during the operation. This is most noticeable in major operations, such as thoracoplasties, mastectomies and arthroplasties. Taking the thoracoplasty as the best index, since there is a large series of cases and it is an operation of considerable magnitude, one finds that the patient seldom shows much systemic reaction other than the drop in blood pressure immediately following operation, and this is soon relieved by transfusion or other intravenous fluid. Convalescence is rapid, and in many cases the next operation is performed after an interval of fourteen days. The best index of the postoperative systemic reaction is probably the elevation of temperature (tables 3, 4 and 5) and the duration of this elevation (tables 6, 7 and 8). In my opinion, however, improvement in the systemic reaction has been even greater than the change in the extent and duration of elevation in temperature.

CASE 1.—G. B., a white boy aged 16, had an indirect inguinal hernia on the left side which had been present all his life. The hernia was repaired with the patient under nitrous oxide-oxygen anesthesia on November 26, silk being used as a suture material. When the skin sutures were removed on the sixth day the wound was described as well healed. On the twelfth postoperative day, when

TABLE 6.—*Extrapleural Thoracoplasty for Pulmonary Tuberculosis; Duration of Postoperative Temperature Elevation**

Days	Without Radiation		With Radiation	
	No.	Percentage	No.	Percentage
No postoperative elevation.....	2	2.0	42	24.0
1.....	0	0	3	2.0
2.....	1	1.0	39	22.0
3.....	11	10.0	22	13.0
4.....	10	9.0	30	17.0
5- 7.....	35	32.0	24	13.7
8-14.....	39	35.0	9	5.0
15-21.....	6	5.5	3	1.7
22+.....	6	5.5	3	1.7
Total.....	110	100	175	100

* Above 37.5 C. (99.5 F.), or the preoperative level.

TABLE 7.—*Radical Mastectomy; Duration of Postoperative Temperture Elevation**

Days	Without Radiation		With Radiation	
	No.	Percentage	No.	Percentage
No postoperative elevation.....	0	0	1	2.6
1.....	0	0	0	0
2.....	1	7.7	6	15.8
3.....	0	0	12	31.6
4.....	5	38.5	11	29.0
5- 7.....	5	38.5	6	15.8
8-14.....	0	0	1	2.6
15-21.....	1	7.7	0	0
22+.....	1	7.7	1	2.6
Total.....	13	100	38	100

* Above 37.5 C. (99.5 F.), or the preoperative level.

TABLE 8.—*Inguinal Herniorrhaphy; Duration of Postoperative Temperature Elevation**

Days	Without Radiation		With Radiation	
	No.	Percentage	No.	Percentage
No postoperative elevation.....	13	8.6	13	15.0
1.....	0	0	2	2.3
2.....	9	6.0	13	15.0
3.....	22	14.6	30	34.5
4.....	37	24.5	17	19.5
5- 7.....	55	37.0	9	10.3
8-14.....	13	8.6	3	3.4
15-21.....	1	0.7	0	0
22+.....	0	0	0	0
Total.....	150	100	87	100

* Above 37.5 C. (99.5 F.), or the preoperative level.

the dressing was again removed, there was some separation of the edges of the skin, with a raw area from which *Staph. aureus* was cultured. There was no evidence of infection below the surface. The patient was discharged the following day. The postoperative temperature curve is shown for the first eight days (chart 1). It remained normal throughout the remainder of the patient's stay in the hospital. This case probably should not be classed as one of infection.

CASE 2.—M. H., a Negress aged 51, married, had a carcinoma of the breast, of sixteen months' duration. She had received eighteen roentgen treatments, and areas of skin had lost their pigmentation as a result of the blisters following these treatments. A radical mastectomy was performed on February 15. The postoperative temperature for the first eight days is given in chart 2. During the remainder of the stay in the hospital the temperature was normal. On the eighth day an abscess was found about a single stay suture which passed through the axillary hair-bearing skin. The remainder of the incision was free of any infection, and the abscess healed promptly, with little drainage, after removal of the offending stay suture.

CASE 3.—D. C., a white woman aged 31, single, had a history of bilateral pulmonary tuberculosis of eight years' duration. Cavitation in the left lung had been present for the past four years. An extrapleural paravertebral thoracoplasty was performed on June 15. The operator's glove was torn during the operation, and gross inoculation of the wound with a considerable quantity of contaminated perspiration occurred. The wound was immediately and thoroughly washed out with physiologic solution of sodium chloride. A rapid rise of temperature followed operation, with evidence of wound infection (chart 3). The wound was opened six days after operation, for free drainage. Cultures showed *Staph. aureus haemolyticus*. Healing progressed satisfactorily and the remaining ribs were subsequently resected.

CASE 4.—S. P., a white woman aged 32, single, had a history of tuberculosis of six years' duration and had had eleven ribs resected four years before admission. On October 1 an extrapleural paravertebral thoracoplasty was performed through the scar from the previous operation. The three upper regenerated ribs were resected. After the operation the temperature did not go above 38 C. (100.4 F.) and was down to normal within forty-eight hours (chart 4). After the operation the patient lay on her back during warm weather and perspired freely. The dressings slipped, the upper end of the incision being exposed. The silk skin sutures were not removed until the ninth day, at which time there was some superficial maceration at the upper end of the incision, with cutting of the silk sutures. Cultures taken from the suture line showed a growth of *Staph. aureus*. The incision was described as healed on the twelfth postoperative day, and there was no elevation of temperature before the next operation (see report of case 5). The infection in this case probably was not an operating room infection.

CASE 5 (same patient as in case 4).—On October 15 a second stage extrapleural paravertebral thoracoplasty was performed through the incision for the first stage, with lengthening of the incision at the lower end. The regenerated fourth, fifth, sixth and seventh ribs were resected. After the operation the temperature did not go above 37.5 C. (99.5 F.) at any time (chart 5). The patient again lay on her back and perspired freely. The silk skin sutures were removed on the eighth day after the operation. There were numerous pustules about the sutures at this time. Cultures of pus from these showed *Staph. aureus*.

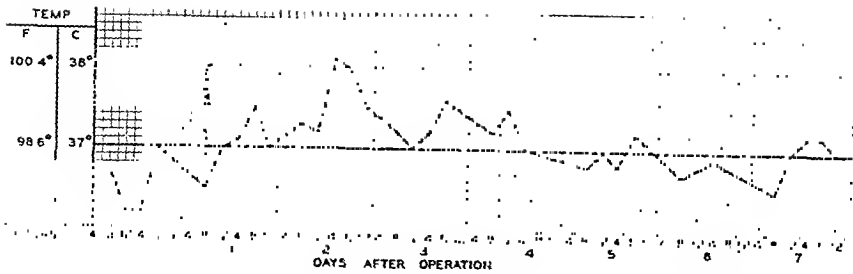


Chart 1.—Temperature chart of the patient in case 1.

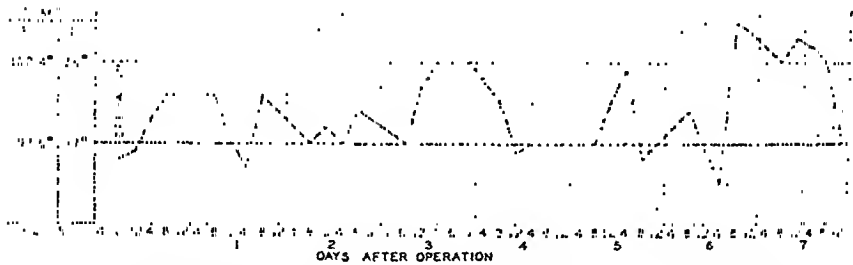


Chart 2.—Temperature chart of the patient in case 2. Radical mastectomy was the operation performed.

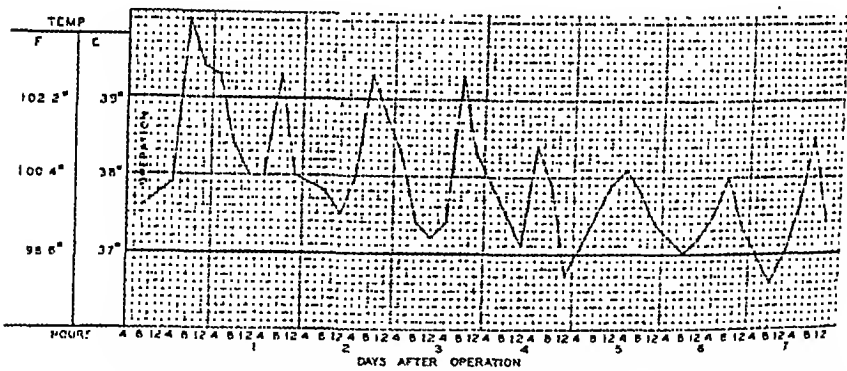


Chart 3.—Temperature chart of the patient in case 3. An extrapleural paravertebral thoracoplasty was performed.

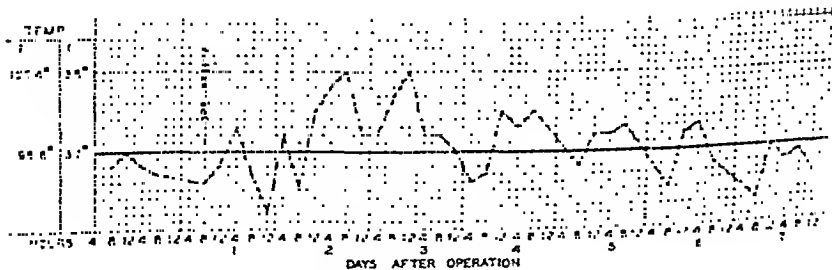


Chart 4.—Temperature chart of the patient in case 4. The first stage of an extrapleural paravertebral thoracoplasty was performed.

Practically all of these were healed two days later, but there was a small amount of drainage from the upper end of the incision. Photographs taken twelve days after operation showed the wound well healed, and the patient was discharged two and one-half weeks after the second operation. There was no elevation of temperature during the hospital stay after that shown on chart 5. The condition in this case probably was not an operating room infection but multiple stitch abscesses.

CASE 6.—S. G., a white man aged 23, single, showed, in addition to bilateral pulmonary tuberculosis of three years' duration with cavitation on the left, marked anene, with a pustular eruption over the back. Operation was delayed until the sixth day after admission in order that the cutaneous infection might be treated. On August 7 an extrapleural paravertebral thoracoplasty was performed on the left side, with resection of the first, second, third and fourth ribs. The incision was made with the surgical diathermy in the hope that it would be less likely to carry organisms into the wound. (I feel that this was false reasoning and that such a procedure probably gave the organisms more dead tissue in which to grow.) The cutaneous incision was closed with buried sutures of catgut and skin sutures of silk. The dressings slipped, and the upper end of the incision was exposed. Healing was delayed because of damage to the



Chart 5.—Temperature chart of the patient in case 5 (the same patient as in case 4) after the second stage of the operation.

skin by the cutting current. A low grade superficial infection developed (chart 6). This healed before the second operation, thirty-five days after the first stage.

CASE 7 (same patient as in case 6).—The patient had a pustular eruption on the back, and there had been superficial infection at the first stage (chart 6). On September 10 the second stage of the thoracoplasty was performed through the scar from the first stage. The fifth, sixth, seventh and eighth ribs were resected. For twelve days after operation the temperature did not go above 38 C. (100.4 F.) except for the one point shown on chart 7. The sutures were removed on the ninth day, and the wound was described as well healed, with no infection. There was one recorded temperature daily above 38 C. (100.4 F.) on the fifteenth, sixteenth and seventeenth days after the second operation, and a hematoma was aspirated at this time. Dark brown, syrupy fluid was obtained. The culture was lost. Two small draining sinuses opened at the lower end of the incision by the twenty-fourth day after operation, but these drained only a slight amount of serosanguineous fluid.

The temperature remained irregularly elevated to above 38 C. (100.4 F.) daily. The wound was explored on the twenty-eighth day, but no pus was found, and there was little subsequent drainage from this incision, which was left open. The wound and sinuses healed by the twenty-ninth day after it was

and the twelfth day, at which time the lower end of the incision was opened, a walled-off pocket of pus was evacuated and drains were inserted. The temperature dropped to normal within twelve hours and remained normal. Nine days after the abscess was drained, the patient had a sudden pain in the chest while straining in getting off a bedpan and died within a few minutes. Autopsy confirmed the diagnosis of pulmonary embolus. The wound had healed except for a small granulating area at the drainage site.

CASE 9.—M. G., a white woman aged 34, married, had a history of tuberculosis of the left lung of twenty-nine months' duration. Her general condition was good. There was a history of an acneform eruption during the menstrual periods.

The second stage extrapleural paravertebral thoracoplasty was performed fourteen days after the first stage, through the old incision. The fourth, fifth and sixth ribs were removed. Two hundred to 300 cc. of old blood was found beneath the scapula. The temperature had remained normal except for two days after the first operation. Immediately after the second stage it rose and remained elevated until a subcapsular abscess was drained (chart 9). This

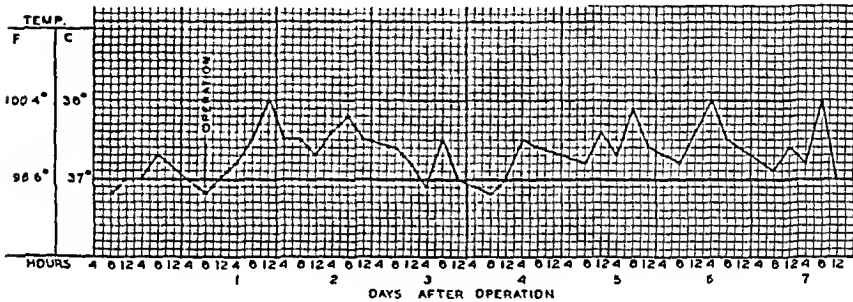


Chart 8.—Temperature chart of the patient in case 8 after reopening of the incision for the second stage of an extrapleural paravertebral thoracoplasty.

wound apparently became infected at the time of the second operation. The organisms may have gained entrance to the subcutaneous fat along the skin sutures for the first stage of the operation.

CASE 10.—J. W., a white man aged 23, single, had a history of tuberculosis of the left lung of three years' duration. The entire lung was fibrosed, and there was a cavity in the apex. The second stage extrapleural paravertebral thoracoplasty was performed twenty-one days after the first stage, through the original scar with removal of four ribs at each stage. (For the temperature curve following the second stage see chart 10.) A small collection of pus in the subcutaneous fat was discovered and drained on the sixth day after the operation. Culture showed *Staph. aureus*. The temperature curve subsequent to that shown in chart 10 was normal, but it required twenty days for the abscess cavity to granulate and the skin to heal over.

CASE 11.—R. C., a white woman aged 42, married, had a history of bilateral pulmonary tuberculosis of eighteen months' duration, with activity on the left. After the first stage, with removal of the first, second and third ribs, the temperature did not go above 37.8 C. (100 F.). While there was nothing to suggest infection, a culture of material from about the skin sutures showed a positive growth of *Staphylococcus albus*. The second stage was performed fifteen days

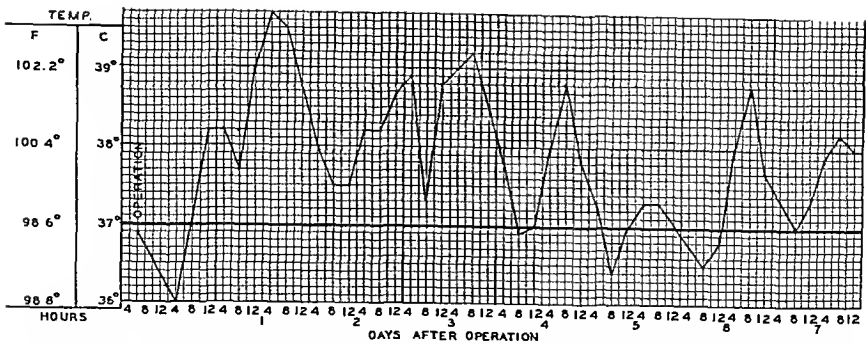


Chart 9.—Temperature chart of the patient in case 9 after reopening of the incision for the second stage of an extrapleural paravertebral thoracoplasty.

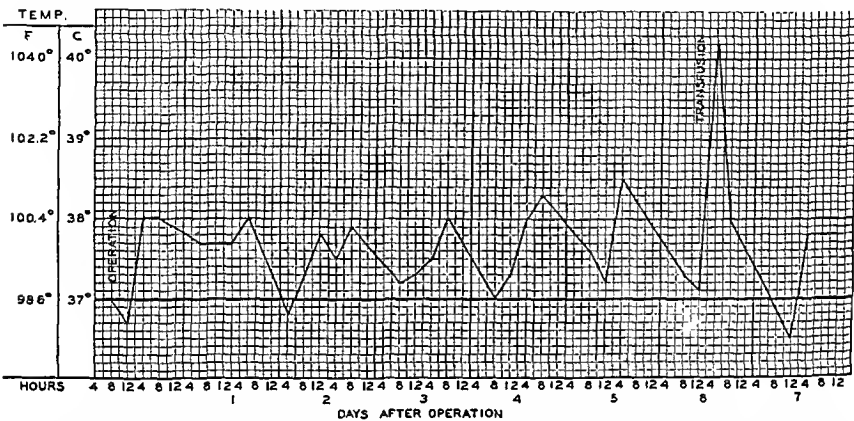


Chart 10.—Temperature chart of the patient in case 10 after reopening of the incision for the second stage of an extrapleural paravertebral thoracoplasty.

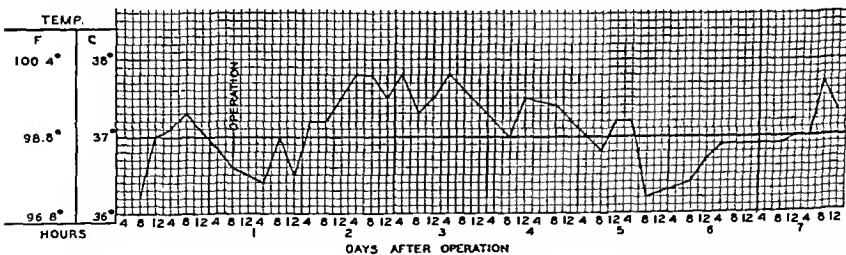


Chart 11.—Temperature chart of the patient in case 11 after reopening of the incision for the second stage of an extrapleural paravertebral thoracoplasty.

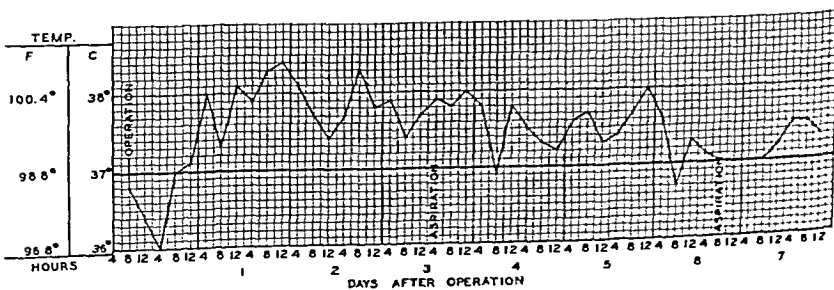


Chart 12.—Temperature chart of the patient in case 12 after the second reopening of the incision for the third stage of an extrapleural paravertebral thoracoplasty.

after the first. The incision was through the scar of the first stage, and parts of the fourth, fifth and sixth ribs were removed. The temperature (chart 11) did not go above 37.8 C. (100 F.). On the eighteenth day after operation a few drops of pus were expressed from the wound. The wound was opened, and pus (*Staphylococcus albus* and *Staph. aureus*) was found to be located about a buried silk suture. This was removed, and healing followed.

CASE 12.—P. M., a white woman aged 37, single, had a history of pulmonary tuberculosis of five years' duration. The disease was bilateral, well healed on the right but with several cavities on the left. The thoracoplasty was performed in three stages at fourteen day intervals. After the first and second stages the temperature remained between 37 and 38 C. (98.6 and 100.4 F.) and after each was normal four days after the operation. At the third operation smears of material from the superficial tissues at the level at which the skin sutures passed through the superficial fat showed an occasional coccus. After this operation the temperature went slightly higher (chart 12). A hematoma was aspirated on the third and seventh postoperative days. From material obtained by the second aspiration *Staph. aureus haemolyticus* was grown. A small opening was made for drainage and irrigation. Healing was satisfactory.

SUMMARY

This study of 456 clean primary incisions and 86 reopened incisions supposedly clean, out of a total of over 800 operations performed in a field of air sterilized by bactericidal radiation, demonstrates:

1. Reduction in the number of postoperative wound infections of over 85 per cent.
2. Elimination of the occasional death from wound infection.
3. Reduction in the number of patients with a postoperative temperature above 38 C. (100.4 F.) as follows:

Thoracoplasties, from 68 to 30 per cent.

Radical mastectomies, from 46 to 34 per cent.

Inguinal herniorrhaphies, from 36 to 22 per cent.

4. Reduction in the number of patients with a temperature elevation above 37.5 C. (99.5 F.) for more than four days after operation as follows:

Thoracoplasties, from 78 to 22 per cent.

Radical mastectomies, from 54 to 21 per cent.

Inguinal herniorrhaphies, from 46 to 14 per cent.

5. Improvement in wound healing.
6. Lessened systemic reaction.
7. Shortened convalescence.

CONCLUSIONS

The air in the operating room, as previously reported,² is highly contaminated with pathogenic bacteria.

This air is an important source of contamination in every operative wound.

Sterilization of the air in the operating room can be accomplished by means of bactericidal radiation, as previously reported.

With meticulous operating room asepsis, development of a delicate atraumatic technic, the use of the least irritating suture material, and the elimination of air-borne contamination of the operative wound and sterile supplies by the use of bactericidal radiant energy, wound infections in clean primary incisions may be almost eliminated.

Bacteria from the hair follicles and glands in the skin, breaks in technic or blood-borne bacteria from a focus elsewhere in the body are at present the only sources of infection of clean operative wounds.

END RESULTS IN CASES OF FIBROSARCOMA OF THE EXTREMITIES

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NEW YORK

Rules for the treatment of neoplastic disease must be based on carefully considered case reports in which complete data on the pathologic picture, clinical development, course, history and end results, to the death of the patient or at least to the end of a five year follow-up, are available to the reporter. The inclusion of cases in which the original diagnosis was made by an unknown pathologist is subject to the criticism that the pathologist may not have been expert in the diagnosis of tumor. The inclusion of cases dating to a previous decade is questionable unless the early slides can be reviewed, since the classification of many tumors has undergone extensive change in recent years. Reports of diagnoses made after biopsy of material taken by means of a punch or by aspiration, without subsequent study of additional tissue, are of questionable value. When the cause of death within a five year period is surmised or unknown the case should be excluded, since a patient with neoplastic disease may live for three years or more after operation and finally die from a cause unrelated to the tumor. The duration of tumor before operation must be known, since with the recent increase in "tumor consciousness" on the part of physicians and the laity the lesions are being seen in earlier stages than they were generally seen in the past. Prognosis may perhaps be comparatively more favorable for tumors of relatively recent occurrence.

These difficulties are particularly significant when an attempt is made to formulate rules for the treatment of fibrosarcoma of the extremities. Such a tumor, while not rare, is not sufficiently common to furnish a large series of complete cases to any one author. The classification of the sarcoma group has until recently been almost chaotic. Pathologic interpretation of sarcoma tissue requires extremely careful consideration since for the most part such tissue does not present characteristic cell formation as does that of certain other common neoplasms.

I have attempted to meet these requirements in a series of cases observed during the past five years. Complete data have been accumulated on 20 cases. Reports of 4 additional cases have been appended, for which five year end results or death have not been as yet recorded

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but which have been followed to a point at which the course was in complete accord with that of the cases in the first series. Before the cases are listed a clear definition of terms must be offered.

A fibroblastic tumor is a neoplasm of mesodermal origin, composed of cells whose ultimate function is the production of fibrous connective tissue. These tumors vary in structure within the limits of precursing tissue architecture and within the limits of adult connective tissue variations.¹

In its malignant form such a tumor is designated by the term fibrosarcoma. Histologic variants, such as fibromyosarcoma, so-called angiofibrosarcoma and neurofibrosarcoma, present no differences in clinical development, subsequent course or response to treatment. (In order to avoid repetition the reader is referred to a previous paper for elucidation of these statements.²)

REPORT OF CASES

CASE 1.—A woman aged 50 presented herself with a spindle cell fibrosarcoma on the foot, involving the subcutaneous fibrous tissue and tendon sheaths. The duration of the tumor was given as ten months. Attempts at aspiration had been made elsewhere on three occasions before her admission. The growth was increasing. A biopsy specimen was finally excised on March 9, 1933. Twenty-one days were spent in confirming the diagnosis. Amputation above the knee was performed on March 30. The lungs were not involved, as far as could be determined by roentgen study. The patient died May 25, about two months after the amputation. The lungs were apparently clear; at least, they were not grossly involved. There were metastases to the liver.

CASE 2.—A woman aged 21 came to the hospital with a fibrosarcoma originating in muscle or subsynovial connective tissue. The tumor was located chiefly within the gastrocnemius muscle, near the popliteal space. The primary tumor had been discovered in 1934, when it apparently had broken through to the subcutaneous tissue, presenting a visible mass. It was excised at that time. Subsequent observation showed that the primary excision was probably incomplete. The tumor recurred to clinically observable proportions within a few months. Secondary excision was attempted in June 1935. A third excision for secondary recurrence was found necessary in January 1936. This was followed by high voltage roentgen irradiation, 200 kilovolts at a distance of 50 cm., filtered with 0.5 mm. of copper. Treatment was given for fifty days; three fields were used around the knee and lower femur. Two thousand roentgens was given to the posterior field, 2,000 to the inner field and 2,250 to the popliteal space. The treatments were given practically daily in divided doses. Amputation was performed at the level of the upper part of the thigh on October 30. The patient died in April 1937. The lungs were roentgenologically normal before amputation but showed metastases before death.

CASE 3.—A man aged 50 presented a spindle cell fibrosarcoma on the anterior surface of the thigh, involving the fascial tissues. The duration of the tumor

1. Bick, E. M.: Fibroblastic Tumors of the Extremities, *Arch. Surg.* **35**:841 (Nov.) 1937.

2. Bick, E. M.: Fibrosarcoma of the Extremities, *Ann. Surg.* **101**:759, 1935.

was three years. It had been excised twice during this period before the present admission. Amputation was performed through the upper portion of the thigh in February 1934. Roentgen examination before the amputation showed no abnormality of the chest. The patient died from metastases in August.

CASE 4.—A man aged 48 presented himself with a spindle cell fibrosarcoma involving the fibula and the lateral surface of the leg. The tumor apparently originated from the periosteum. The duration of symptoms was three years. He had undergone primary excision before admission. Amputation at the level of the upper part of the thigh was performed in November 1936. The patient died early in 1937. Roentgenograms of the chest showed no abnormality before amputation. The primary tumor had not been recognized as involving bone; hence it had been incompletely excised.

CASE 5.—A man aged 42 presented a spindle cell fibrosarcoma originating in the subsynovial connective tissue at the level of the knee. A primary tumor had been excised two years before the present admission. The present admission was for a first recurrence. Amputation at the upper part of the thigh was performed in August 1928. The patient was living and well in September 1935.

CASE 6.—A woman aged 60 presented a spindle cell fibrosarcoma on the posterior aspect of the thigh, of fascial origin. The duration of the tumor was given as five months. The primary tumor was excised in September 1926; the first recurrent growth was excised in April 1927, and a second recurrent growth was declared inoperable in September. Roentgen examination showed metastases to the lungs in November. The patient died in March 1928.

CASE 7.—A woman aged about 30 presented a spindle cell fibrosarcoma, possibly of nerve sheath origin, from the region of the shoulder, involving the subcutaneous connective tissues. It was excised in November 1929; the operation was followed by a course of irradiation. The patient was living and well in January 1936.

CASE 8.—A woman aged 31 presented a fibrosarcoma of fascial origin in the thigh. The primary tumor appeared in 1924. It was excised and treated with irradiation, but it recurred. A second excision was performed in 1925, with further irradiation. The neoplasm again recurred; a third excision was performed in 1926; further irradiation was given. In October 1927, after a fourth recurrence, the growth was declared inoperable. Two weeks before the last recurrence a tumor was found in the abdomen. The patient died in November 1927, of general sarcomatosis.

CASE 9.—A man aged 75 presented a spindle cell fibrosarcoma involving the deep connective tissue of the heel. The primary tumor was found in 1926 and was excised. It recurred immediately and was again excised; a further recurrence (present admission) took place during December 1928. The tumor was again excised. The patient died in February 1930, of general sarcomatosis.

CASE 10.—A man aged 52 had a pleomorphic fibrosarcoma involving the fascial and deep fibrous tissues of the forearm. The tumor had been present two years before this admission. Primary excision was performed in 1932 and was followed by irradiation. However, the dose was never over 750 roentgens in divided doses. Histologically the tumor was classified as a fibromyxomatous type of fibrosarcoma at that time. It recurred and was excised in 1933; further irradiation therapy was employed. It again recurred during 1936 and was again excised. A third recurrent growth, which developed in May 1937, was also excised. The patient has lived five years. Each recurrent tumor has shown a more malignant type of tissue. Amputation has been advocated but declined.

CASE 14.—A girl aged 17 presented a vascular fibrosarcoma (so-called angio-fibrosarcoma or angiosarcoma) located subcutaneously on the foot at the site of a benign nevus. It had first been observed only two weeks previously. It was excised by endotherm knife in 1926. The patient was living and well in December 1936.

CASE 12.—A woman aged 60 had a myxosarcoma involving the deep fascial tissues of the thigh, of six years' duration. It was excised in July 1928. There was no recurrence when the patient was examined in December 1932. She died of an unrelated cause in February 1934, at the age of 66.

CASE 13.—A man aged 22 presented a spindle cell fibrosarcoma of the thigh, involving the deep fascial tissues. The growth was of four years' duration. Excision had been attempted in November 1934 but was incomplete because of anatomic difficulties. Roentgenograms of the chest taken in October 1935 showed no abnormality. Amputation was refused by the patient. He died in 1936, of metastases to the lung.

CASE 14.—A man aged 24 had a spindle cell fibrosarcoma growing from the deep fibrous planes in the vicinity of the knee, of seven years' duration. The primary tumor was excised in February 1934 because of recent acceleration in growth. It recurred, and a secondary excision was performed in November, followed by irradiation. Eight portals of entry were used. One thousand roentgens was given to each of the eight fields, at 180 kilovolts, filtered with 0.5 mm. of copper and 1 mm. of aluminum. The treatment was given over forty-seven days. The distance was 50 cm. The patient died in December 1935, of multiple metastases to the lungs, to the ribs and to the vertebrae.

CASE 15.—A man aged 35 had a fibrosarcoma of nerve sheath origin, attached to the sheath of the sciatic nerve. The duration of the tumor was given as four years. It was excised in September 1930. The patient was living and well in June 1935.

CASE 16.—A man aged 52 had a fibrosarcoma of the thigh, attached to the periosteum of the femur. Its duration was given as one month. It was excised in March 1933. The patient was living and well in November 1937, with no sign of recurrence.

CASE 17.—A woman aged 76 presented a polymorphocellular fibrosarcoma located in the fascial tissues of the thigh at the level of the upper third, of six months' duration. It was excised in December 1927. There was no recurrence. The patient died of bronchopneumonia in August 1931.

CASE 18.—A woman aged 52 presented a fibrosarcoma of the fascial tissues and subcutaneous connective tissues of the leg. The duration of the lesion was given as one year. It was excised in January 1924. Amputation at the level of the midthigh was performed one week later. The patient was living in May 1933 but had been admitted to another institution in January, because of cholecystitis. Roentgen study at that time revealed metastases to the lung. No final pathologic study of these metastases was made. However, the patient was alive and well nine years after the excision of the original tumor, without recurrence.

CASE 19.—A woman aged 41 had a fibrosarcoma involving the connective tissues overlying the deltoid muscle. The duration of the tumor was two years. It was excised in January 1934. The patient was living and well in November 1937.

CASE 20.—A woman aged 39 presented a spindle cell myxofibrosarcoma located in the fascial tissues of the thigh. It was excised in November 1933. The patient was living and well in November 1937.

ADDENDA

CASE 21.—A man aged 50 had a spindle cell fibrosarcoma involving the gastrocnemius muscle. Its duration was given as nine months. It was excised in October 1932, but it recurred. A second excision was effected in December 1933. The growth again recurred, and a third excision was performed in January 1934, followed by irradiation.

CASE 22.—A woman aged 35 had a spindle cell fibrosarcoma of the thigh, involving the deep connective tissues outside the muscle pack. It had first been noted three years previously. It was excised in May 1934. The patient was living and well in November 1937.

CASE 23.—A man aged 34 had a spindle cell fibrosarcoma on the anterior surface of the leg, probably of periosteal origin. It had been present for two years. Amputation was performed in June 1935. The patient was living and well in November 1937.

CASE 24.—A woman aged 31 presented a fibromyxosarcoma located on the leg, originating apparently from the interosseous fibrous tissue. Its duration was given as one and one-half years. It was excised in October 1928 and recurred with gradual acceleration. Amputation was performed in February 1936. The patient was living and well in November 1937.

ANALYSIS OF CASES

The clinical, developmental and pathologic characteristics of fibrosarcoma of the extremities have been presented elsewhere by me and therefore need not be repeated here. The following analysis will be concerned only with the results of treatment in the 20 cases listed in the main series.

Nine patients died as a result of neoplastic disease within a five year period. Eight patients (40 per cent) were alive without perceptible sign of recurrence or metastasis at the end of five years. One patient, a 76 year old woman, died of bronchopneumonia four years after primary excision, with no evidence of recurrence or metastasis of the tumor. Another patient died nine years after an amputation was done for neoplastic disease of questionable nature. A third patient is living at present, five years after the first excision, having suffered four recurrences treated by repeated wide excision and by irradiation. The later sections of tissue show an increasing degree of malignancy. In this case, while life has been extended to the time of writing, the disease has not been arrested.

On 8 of the 9 patients who died within a five year period, two or more excisions had been performed—that is, one or more excisions of locally recurrent tumor before amputation was performed or the tumor declared inoperable. In another case (case 13) excision was incomplete because of anatomic considerations, and amputation, although advised immediately afterward, was refused. In the second exceptional

case (case 4) excision was also incomplete since the tumor had invaded the adjacent fibula, which was not resected at the time. Later amputation did not save this patient. Hence, no patient lived after a recurrence of the tumor when a second excision was performed. High voltage roentgen therapy, used in 6 cases, did not alter the course of the disease. (In 3 cases the type of irradiation was listed. In the other, precise radiotherapeutic data were not available.) Furthermore, for none of the patients who died within the five year period was amputation performed before the appearance of local recurrence or at the time of local recurrence with the exception of the patients in cases 4 and 13, in which primary excision was incomplete.

Of the 8 patients alive without perceptible recurrence or metastasis at the end of five years, 5 were treated by complete surgical excision and 1 by incision with the endotherm knife. In none of these cases did local recurrence appear. Another patient was treated by complete surgical excision of the primary tumor, followed by amputation for a recurrence two years later. Still another patient was treated by complete surgical excision followed by irradiation.

Of the 2 remaining patients, 1 (the patient in case 17) died of an unrelated cause four years after excision without evidence of recurrence or metastasis. Another (the patient in case 18) was a woman aged 52 whose thigh was amputated after a primary excision and who remained alive and well for nine years. She was then admitted to another institution, at the age of 61, because of gastrointestinal symptoms. A clinical diagnosis of cholecystitis was made. Roentgen studies revealed metastatic lesions in the chest. Autopsy was not performed. The origin or nature of the pulmonary metastasis was not determined. The lesions in this case cannot be ascribed to metastases from the amputated leg, occurring nine years later, although the possibility of its representing a single exception to the rule cannot be denied. This rule¹ is that the "expectancy of recurrence (in fibrosarcoma of the extremities) is highest in the first post-operative year and precipitately decreases after that."

In the 4 cases reported in the addenda, the tumor in case 21 recurred after three excisions followed by irradiation; the patient in case 22 is living and well at the time of writing, three and one-half years after primary surgical excision, and the patient in case 23 is living and well two and one-half years after primary amputation. In case 24 a tumor was excised and recurred with a slow rate of growth. The limb was amputated eight years later. The patient is alive and well almost two years later.

COMMENT

If histologic interpretation of the degree of malignancy of a given fibroblastic tumor were a matter of unquestionable accuracy, one could not avoid the conclusion that primary amputation is imperative in the treatment of fibrosarcoma of the extremities. Unfortunately, however, pathologic diagnosis "is not a factual statement; it is an interpretation of histologic appearance and must be so regarded. . . ." ¹ Except for the general proposition that cellular tissues are more apt to be rapidly malignant than are relatively acellular tissues, I have not been able to establish any correlation between the histologic structure of a fibroblastic tumor and its relative malignancy. Hence, the appearance of some degree of cellularity or malignancy in a tissue reported as fibrosarcoma does not mean that the involved limb must be sacrificed to save life. There are listed in this report 7 of 20 cases in which no recurrence appeared within five years after local excision. Furthermore, no patient whose condition was not complicated died after a primary complete excision of a fibrosarcoma of the extremity before the appearance of a local recurrence. Two patients lived five years after amputation for a first local recurrence, and at the time of writing another patient has lived almost two years after amputation for a first recurrence.

Each case of fibroblastic tumor of an extremity presents an individual problem. Is the tumor benign? If it is borderline or obviously malignant, what is its virulence? Is it necessary to amputate? Is irradiation necessary? Can one afford to excise the tumor and continue observation for recurrence? The present work has been carried on for the past six years in the hope of answering these questions. On the basis of 20 complete and 4 partially complete cases carefully studied the following answers are submitted.

CONCLUSIONS

1. For any fibroblastic tumor of the extremity for which complete surgical excision of a primary lesion is anatomically feasible such treatment is indicated. By complete surgical removal is meant not only removal of the visible tumor tissue but removal of enough of the surrounding normal structure to make sure that there is no residue. The extent of the excision cannot be measured in centimeters; it must remain a matter of surgical judgment.

2. When complete surgical excision is not anatomically feasible, amputation of the limb is imperative at the time the primary tumor is judged malignant by competent study of the gross specimens *in situ* and by microscopic study of adequate tissue. This is true regardless of

the degree of malignancy as judged by the pathologist. It will be found that many fibrosarcomas of the deep fascial tissues of the thigh or fibrosarcomas originating in the periosteum of the femur fall within this category; that is, their complete surgical removal is difficult to assure.

3. Amputation is imperative at the first sign of recurrence of a fibrosarcoma.

4. Irradiation technic as applied up to this time has not been proved to alter the eventual outcome in such cases. Fibrosarcoma is resistant to present day radiotherapy.

SENSITIZATION AND DESENSITIZATION OF RABBITS TO HETEROPLASTIC TRANS- PLANTS OF THYROID TISSUE

J. DEWEY BISGARD, M.D.

OMAHA

In man isotransplants transferred directly without conditioning the donor, the recipient or the transplant seldom if ever survive permanently. Many such grafts take temporarily, for periods of three to five weeks, and then disintegrate and disappear. This phenomenon has been attributed to chemical incompatibility, and Holman¹ has presented evidence that it is based on the development of sensitization of the recipient to the foreign tissue. He reported the case of a child who received skin grafts from his mother on two occasions with a few days intervening. Both belonged to the same blood group. Two weeks after the second grafting, not only did the new epithelium which had spread from the grafts and had nearly covered the surface of the granulations melt away leaving only the original grafts, but symptoms of a generalized allergic reaction developed. These symptoms, fever, tachycardia, generalized exfoliative dermatitis or eczema and melena, persisted until the original grafts were removed from the surface with a curet. They then rapidly disappeared. Various attempts to develop a method of adapting the donor, the recipient or the grafts themselves have been made. Among methods investigated are preliminary transfusions of blood and injections of tissue extracts, and more recently tissue culture has been studied by Stone, Owings and Gey.²

With the exception of skin grafts, the transplants in these studies have been buried in muscle or other tissues where encapsulating and invading fibrous tissue has undoubtedly influenced the fate of the grafts. In the investigation reported below the transplants were cultured in the anterior chamber of the eye, and this location was selected because it has been observed in my similar previous studies³ that much less fibrosis occurs in tissue cultured in the anterior chamber.

From the Departments of Surgery and Physiology, School of Medicine, University of Nebraska.

1. Holman, E.: Protein Sensitization in Iso-Skingrafting, Surg., Gynec. & Obst. **38**:100 (Jan.) 1924.

2. Stone, H. B.; Owings, J. C., and Gey, G. O.: Transplantation of Living Grafts of Thyroid and Parathyroid Glands, Ann. Surg. **100**:613 (Oct.) 1934.

3. Bisgard, J. D.: Ossification, Arch. Surg. **33**:926 (Dec.) 1936.

Thyroid and in a few instances ovarian and uterine tissues were used for transplants. These tissues were used for the reasons that they can be identified readily, that their states of cellular activity are reflected to some extent histologically and that some criteria of function of the transplants can be ascertained. Function can be determined in the case of thyroid transplants by the failure of evidence of thyroid deficiency to develop in totally thyroidectomized animals and in the case of utero-ovarian transplants by their reaction to estrogen from the urine of pregnant women injected intravenously. In contradistinction to those in man, heterotransplants in rabbits take readily and apparently function. However, as shown in the following experiments, these animals can be sensitized and desensitized to an individual transplant of tissue.

EXPERIMENTS

In 111 rabbits thyroid tissue was transplanted to the anterior chambers of both eyes. The technic has been described in a previous publication.³ Immediately after removal, the tissue was cut into small bits with a sharp knife, the usual precautions being exercised to avoid trauma, drying and cooling. These fragments were gently threaded into the shaft of a large caliber needle, which was gently forced into the anterior chamber, entering it at the limbus. With the needle in place, the tissue was pushed from the shaft by means of a stilet and deposited in the anterior chamber. By this procedure, only avascular tissue is traumatized and there is no bleeding. Consequently, there is no interference with the "taking" of the graft by interposition of a hematoma. The transplants rapidly establish vascular communications with the iris.

All animals which received thyroid transplants were totally thyroidectomized either before or within a few days after transplantation. As stated previously, this was done to test the function of the grafts, which if functionally active would prevent signs and symptoms of hypothyroidism from developing. These signs are dry scaly skin, loss of most of the hair, some loss of weight, lethargy and hypochromic macrocytic anemia. Determinations of hemoglobin and erythrocyte counts were made on all animals before death except those which died spontaneously. These signs, it was found in a previous hematologic study⁴ on totally thyroidectomized rabbits, developed in 75 per cent of the animals and appeared from eight to ten weeks after total thyroidectomy. The experiments fall into several groups, which will be outlined here and classified in the table. Several grafts were lost through infection of the eyes or inability to locate the grafts at autopsy or in sections, and some were discarded because the animals into which they had been placed died in less than twelve weeks after transplantation.

Group I: Autogenous Transplants.—Autogenous grafts of thyroid tissue were made to both eyes of 4 animals. Examined from fifty-two to one hundred and sixty-eight days later, 7 of the 8 grafts were found attached to the iris, and the tissue of each graft not only was viable but appeared to be hyperplastic. As evidence of hyperplasia the follicles were small and lined with tall cuboidal epithelium, and there was more than a normal quantity of lymphoid tissue. In a few areas thyroid tissue was missing and replaced by fibrous tissue. Since

4. Sharpe, J. C., and Bisgard, J. D.: The Relation of the Thyroid Gland to Hematopoiesis, *J. Lab. & Clin. Med.* 21:347 (Jan.) 1936.

signs of myxedema did not develop in any animal in this group and since the transplanted tissue in each instance was hyperplastic, it would appear that the grafts functioned.

Group II: Isotransplants in Litter Mates.—In the second group transplantations were made directly to litter mates. Nine animals were used, and of the 18 transplants 12 survived, 3 were necrotic and 3 could not be found in the tissue removed at autopsy. The transplants were recovered for microscopic examination from forty-two to one hundred and sixty-six days after transplantation. In 2 animals no viable transplants were found, and in 1 of these signs of myxedema developed. With only 1 exception, the viable transplants found showed evidence not only of functional activity but also of hyperplasia. Photomicrographs of 1 of these transplants appear in figure 1.

In 4 rabbits segments of uterus and ovary from litter mates were transplanted to both eyes. At the same time these animals were totally oophorectomized. Six transplants survived and were histologically viable, as shown in photomicrographs in figure 2, and apparently were functioning one hundred and fifty-seven or one hundred and fifty-nine days after transplantation. In 1 animal both grafts had been replaced by connective tissue. On two occasions, sixty and one hundred and thirty-two days after transplantation, 15 cc. of urine from pregnant women was injected intravenously. Within thirty-six hours the eyes containing viable transplants became slightly injected and began to lacrimate. Some free blood appeared in the anterior chambers, and the transplants reacted as did those described by Allen and Priest.⁵ The ovarian grafts enlarged to several times their original size, and their color changed from pale ivory to bright cherry red. Some tissue, presumably uterine, became pink. After forty-eight hours the reaction gradually regressed, and the ovarian transplants became salmon colored and finally ivory gray.

From these observations it would appear that heterotransplants in the rabbit not only survive transplantation in a large percentage of instances but also continue to function.

Group III: Isotransplants from Different Species of Rabbits.—Five albino rabbits received transplants from Belgian hares. Examined eighty-six to two hundred days later, 1 graft had been replaced by fibrous tissue and 5 were viable. Two of these showed hyperplasia. In 2 animals and in 1 eye of a third no thyroid tissue was found, probably as a result of inability to locate grafts in 3 eyes, loss from infection in 1 and loss from necrosis in 1. Myxedema developed in 1 rabbit. Thus 5, or 50 per cent of the total and 83 per cent of the 6 grafts recovered, survived and presumably functioned.

Group IV: Isotransplants of Thyroid Tissue of Dogs to Rabbits.—Four rabbits received transplants of thyroid tissue from dogs. At autopsy fifty-seven or one hundred and forty-four days later, no grafts could be found in 4 eyes. In the other 4 there was only necrotic and fibrous tissue. All eyes showed moderate inflammation for some time after transplantation. In all but 1 of these rabbits signs of myxedema developed. Thus there was both histologic and physiologic evidence that the grafts had failed to survive.

Group V: Isotransplants After Sensitization and Desensitization of the Recipient by Injections of the Donor's Blood.—A. Massive Injections of Blood

5. Allen, E., and Priest, F. O.: Physiological Response of Ectopic Ovarian and Endometrial Tissue, Surg., Gynec. & Obst. 55:553 (Nov.) 1932.

Results of Experiments

Experiment	Rabbit No.	Injections of Blood		Tissue Extract Pre-operative	Condition of Graft			Duration of Graft, Days	Hypothyroidism	Percentage of Takes
		Pre-operative	Post-operative		Lost	Neerotic	Viable			
Group I										
Autogenous grafts of thyroid	3	0	0	0	1	0	2H*	168	0	
	6	0	0	0	0	0	2H	112	0	
	19	0	0	0	0	0	2H	115	0	
								52	0	88
Group II	9	0	0	0	0	0	2H	42	0	
Isografts of litter mates' thyroid	18	0	0	0	0	1	1H	136	0	
	43	0	0	0	0	0	2H	119	0	
	45	0	0	0	1	1	0	139	+	
	55	0	0	0	1	1	0	141	0	
	90	0	0	0	1	0	1	166	0	
	121	0	0	0	0	0	2H	95	0	
	10	0	0	0	0	0	2H	130	0	
	5	0	0	0	0	0	2H	111	0	67
Group II	2	0	0	0	0	0	2	157	++	
Isografts of litter mates' uterus and ovary	4	0	0	0	0	0	2	157	++	
	52	0	0	0	0	0	2	159	++	
	68	0	0	0	0	2	0	159	0	75
Group III	20	0	0	0	1	1	0	157	+	
Isografts of thyroid of a different species of rabbit	21	0	0	0	2	0	0	157	0	
	34	0	0	0	0	0	2	155	0	
	35	0	0	0	1	0	1	200	0	
	42	0	0	0	0	0	2H	86	0	50
Group IV	70	0	0	0	1	1	0	144	+	
Isografts of thyroid of a dog to a rabbit	71	0	0	0	2	0	0	144	+	
	72	0	0	0	0	2	0	57	0	
	73	0	0	0	1	1	0	144	+	0
Group V A	38	2	0	0	1	1	0	111	0	
Isografts of thyroid after the injection of 10 cc. of the donor's blood in a single dose	78	2	0	0	0	2	0	118	+	
	11	1	0	0	0	2	0	125	+	
	12	1	0	0	0	2	0	125	+	
	13	3	0	0	0	2	0	112	0	
	14	3	0	0	0	2	0	123	+	
	57	6	0	0	0	2	0	142	+	
	79	6	0	0	0	2	0	115	0	0
Group V B	02	7 daily	0	0	1	1	0	69	0	
Isografts of thyroid after daily injections of 0.2 cc. of the donor's blood to recipient	EI	7 daily	0	0	1	1	0	150	+	
	117	7 daily	0	0	1	1	0	108	0	
	36	7 daily	0	0	0	2	0	115	+	0
	39	14 daily	0	0	0	2	0	99	+	
	37	14 daily	0	0	0	2	0	146	+	
	40	14 daily	0	0	1	1	0	130	+	0
	41	28 daily	0	0	0	0	2H	88	0	
	46	28 daily	0	0	2	0	0	110	0	50
Group V C	74	25 daily	0	0	1	1	0	86	0	
Isografts of thyroid of a dog to a rabbit after daily injections of 0.2 cc. of the donor's blood to the recipient	76	25 daily	0	0	0	2	0	55	0	0
Group V D	64	0	5	0	0	2	0	136	+	
Isografts followed by the injection of 10 cc. of the donor's blood to the recipient in a single dose postoperatively	80	0	5	0	2	0	0	120	0	
	83	0	5	0	0	0	2H	248	0	
	65	0	21	0	0	2	0	136	0	
	67	0	42	0	0	2	0	118	+	
	86	0	42	0	0	2	0	166	+	
	87	0	42	0	0	0	2H	215	0	29
Group VI	88	7 daily	0	0	0	1	1	121	+	
Isografts of thyroid after daily injections of 0.2 cc. of the recipient's blood to the donor	103	7 daily	0	0	0	2	0	120	+	
	60	14 daily	0	0	0	2	0	121	+	
	62	14 daily	0	0	0	2	0	117	+	
	51	14 daily	0	0	1	1	0	52	0	10
	49	28 daily	0	0	1	1	0	70	0	
	53	28 daily	0	0	1	0	1H	121	0	25

* H signifies hyperplastic condition.

† Positive Aschheim-Zondek tests were made on the rabbits thus marked.

Results of Experiments—Continued

Experiment	Rabbit No.	Injections of Blood		Tissue Extract Pre-operative	Condition of Graft			Duration of Graft, Days	Hypothyroidism	Percentage of Takes
		Pre-operative	Post-operative		Lost	Necrotic	Viable			
Group VII	28	7 daily	0	0	0	2	0	149	+	
Isografts of thyroid after reciprocal daily injection of 0.2 cc. of blood	23	7 daily	0	0	0	2	0	64	0	
	29	7 daily	0	0	1	1	0	149	+	0
	24	14 daily	0	0	0	2	0	108	0	
	25	14 daily	0	0	0	2	0	143	+	
	31	14 daily	0	0	0	2	0	94	0	0
	26	28 daily	0	0	1	1	0	128	0	
	32	28 daily	0	0	0	2	0	128	+	
	27	28 daily	0	0	0	2	0	128	+	
	33	28 daily	0	0	1	0	1H	159	0	12.5
Group VIII	118	7 daily	0	0	0	2	0	130	0	
Isografts of thyroid (1) after preliminary daily injections of 0.2 cc. of nonspecific blood	119	7 daily	0	0	0	0	2	130	0	
	02	7 daily	0	0	1	0	1	69	0	
	112	14 daily	0	0	0	0	2	130	0	
	113	14 daily	0	0	1	1	0	126	0	
(2) followed by 10 cc. of nonspecific blood in a single dose	114	0	7 (single inj.)	0	0	0	2H	93	0	
	115	0	7 (single inj.)	0	0	1	1	95	0	57
Group IX A	94	0	0	0	0	2	0	120	0	
The injection of isografts of human thyroid to a rabbit	97	0	0	0	0	2	0	21	0	
	98	0	0	0	1	1	0	37	0	
	99	0	0	0	1	1	0	28	0	
	100	0	0	0	0	2	0	42	0	
Group IX B	95	28 daily	0	0	0	2	0	31	0	
Isografts of human thyroid to a rabbit after daily injections of 0.2 cc. of blood	96	28 daily	0	0	0	2	0	61	0	
	109	28 daily	0	0	1	1	0	21	0	
	110	28 daily	0	0	0	2	0	26	0	0
Group X	3B	0	0	7 daily	0	1	1H	101	0	
Isografts of thyroid after daily injections of extract of the donor's thyroid	4B	0	0	7 daily	1	1	0	99	+	
	5B	0	0	7 daily	2	0	0	85	0	17
	6B	0	0	14 daily	0	2	0	120	+	
	7B	0	0	14 daily	1	1	0	110	0	
	12B	0	0	14 daily	0	0	2H	110	0	
	15B	0	0	14 daily	0	2	0	94	+	
	16B	0	0	14 daily	0	2	0	110	0	
	17B	0	0	14 daily	0	2	0	80	0	
	18B	0	0	14 daily	1	1	0	90	+	
	20B	0	0	14 daily	1	0	1H	92	0	19
	27B	0	0	22 daily	0	0	2H	110	0	
	29B	0	0	22 daily	0	2	0	100	0	
	30B	0	0	22 daily	0	1	1	110	0	
	34B	0	0	22 daily	0	0	2H	110	0	63

from the Donor of the Tissue Before Transplantation: Eight rabbits were given 10 cc. of blood in one injection (some intravenously) and one, two, three and six days later received transplants of thyroid tissue from the animals from which they had received blood. When they were examined, from one hundred and eleven to one hundred and forty-two days subsequently, no viable transplanted tissue was found. In 15 instances it appeared that the grafts had become necrotic and been replaced by fibrous tissue. In 5 of the 8 animals myxedema developed.

B. Repeated Small Injections of the Donor's Blood: Nine rabbits were given daily injections of 0.4 cc. of laked blood (composed of equal parts of water and blood) intramuscularly for periods as listed and then received thyroid transplants from their respective donors of blood. Autopsies were performed on the animals from sixty-nine to one hundred and fifty days later.

1. Four received daily injections for one week; no viable thyroid tissue was found, and 5 grafts had been replaced by fibrous tissue. In 2 of the rabbits myxedema developed.

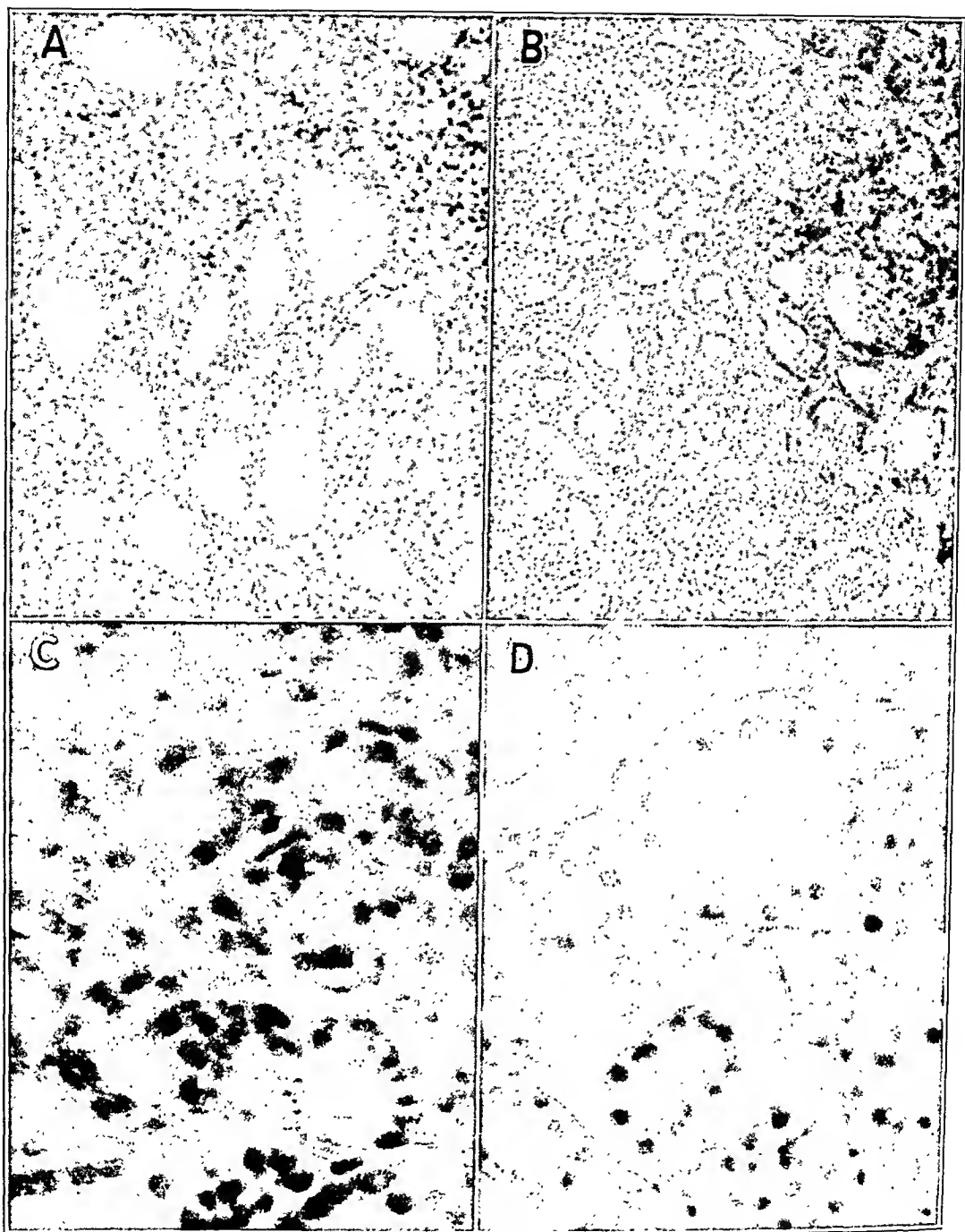


Fig. 1.—*A* and *C*, rabbit 43, group II, isotransplant of one hundred and nineteen days, showing evidence of hyperplasia as compared to *B* and *D*, normal thyroid tissue of a rabbit. Note that the follicles are smaller and more numerous and closely packed, the epithelial cells larger and more cuboidal and the interstitial tissue much diminished. There was also an abnormal abundance of lymphoid tissue, which is not apparent in the field photographed.

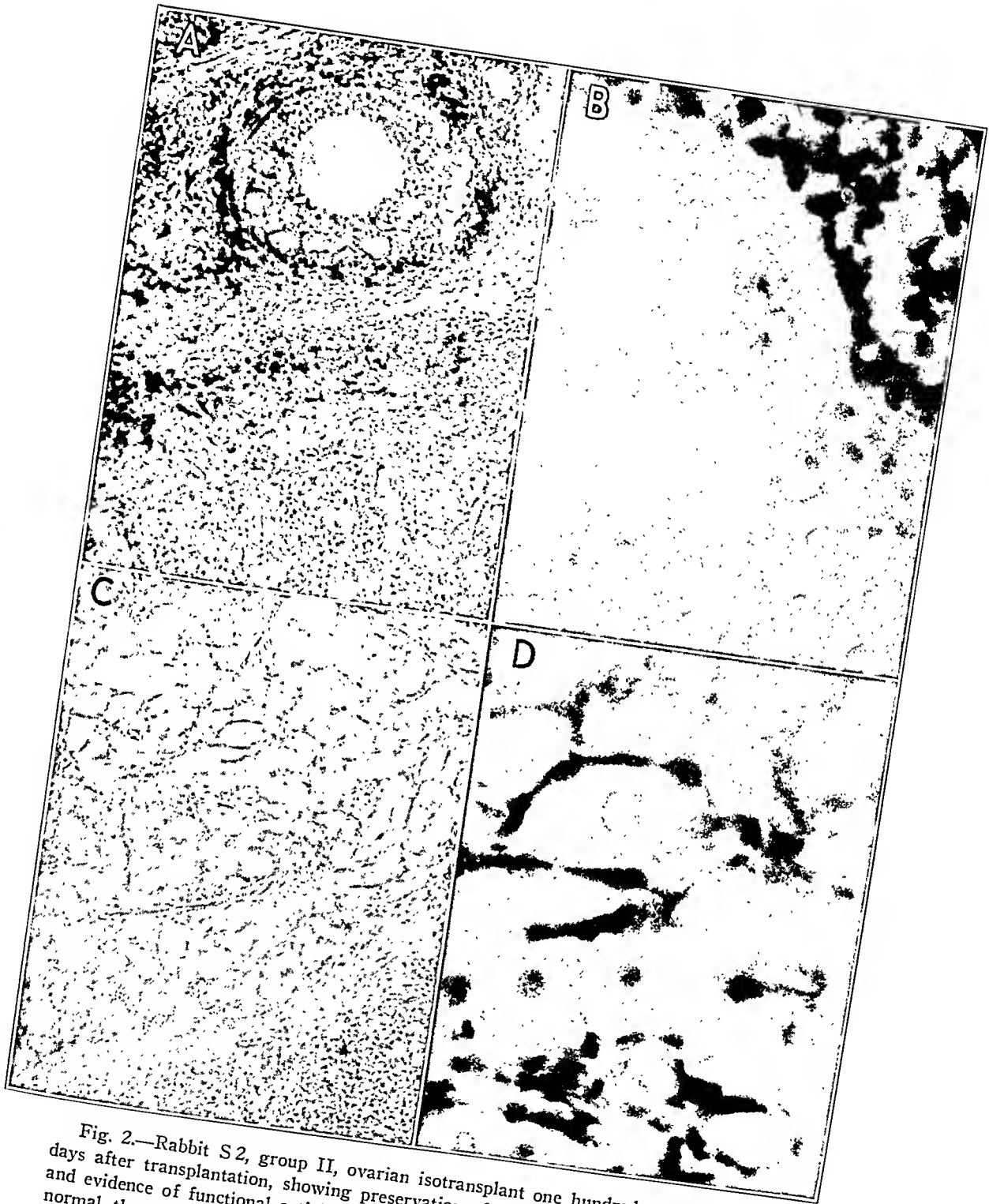


Fig. 2.—Rabbit S2, group II, ovarian isograft one hundred and fifty-nine days after transplantation, showing preservation of its normal histologic structure and evidence of functional activity. *A*, stroma and graafian follicle; *B*, ovum and normal thecal cells; *C* and *D*, low and high magnification of the tissue of the corpus luteum.

2. Three rabbits had daily injections for two weeks. No viable transplants were found, and in 5 instances the grafts had been replaced by fibrous tissue. Myxedema developed in all 3.

3. Two rabbits received daily injections for four weeks, and in 1 both transplants were not only viable but hyperplastic. No signs of hypothyroidism developed in either animal, the takes representing 50 per cent.

C. Repeated Small Injections of the Donor's Blood from Dog to Rabbit: Two rabbits were given daily injections of laked blood for twenty-five days from a dog from which they then received thyroid transplants. None of the 4 grafts survived, and the tissue fifty-five and eighty-six days, respectively, after transplantation was almost entirely necrotic and surrounded by inflammatory tissue. In neither rabbit, however, had myxedema developed.

D. Massive Injections of Blood from the Donor of the Tissue After Transplantation: After receiving transplants 7 rabbits were given 10 cc. of whole blood

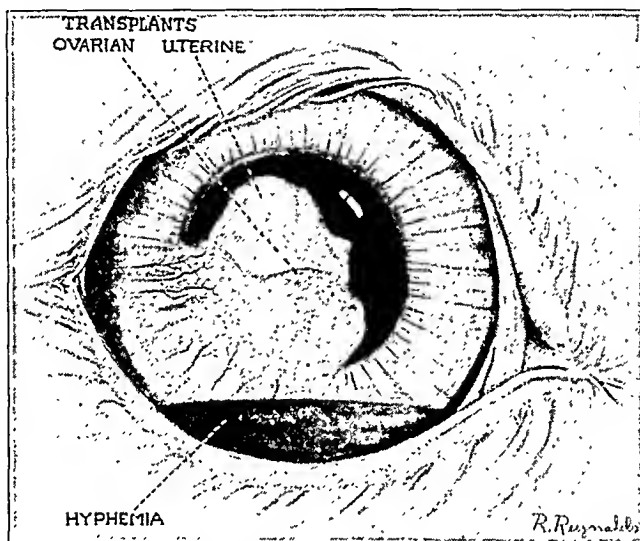


Fig. 3.—Drawing of a utero-ovarian transplant in the anterior chamber, showing the reaction to the injection of 15 cc. of urine of a pregnant woman. (Allan and Priest have reported identical observations.) Note the injection of the iris and the hemorrhage into the chamber. The blushing of the transplant cannot be shown. In the same way transplants of thyroid tissue became attached to the iris and from it received their blood supply.

intramuscularly in a single injection from the animals from which they had received the grafts. These injections were given as follows:

1. Ten cubic centimeters of whole blood to each of 3 rabbits five days after transplantation. Two grafts were viable two hundred and forty-eight days later; 2 were replaced by fibrous tissue, and 2 could not be found, when the animals were examined one hundred and thirty-six and one hundred and twenty days later, respectively. In 1 rabbit myxedema developed.

2. Ten cubic centimeters to 1 rabbit three weeks after grafting. Both grafts were replaced by fibrous tissue.

3. Ten cubic centimeters to each of 3 rabbits six weeks after transplantation. In 1 both grafts survived and were hyperplastic. In each of the other 2 the tis-

sue had been absorbed and replaced by fibrous tissue, and in both signs of myxedema developed.

In this series 29 per cent of the grafts survived.

From this group of experiments it appears that preliminary injections of blood either in a single massive dose or in repeated small injections over a period of less than three weeks serves to sensitize the recipient to the tissue of the donor of the blood, and the grafts fail to take. If the daily injections are continued for three weeks or longer sensitization is lost and the grafts take in a normal percentage of instances. Blood administered after the transplants had established vascular attachments seemed to have exerted a similar influence, though less consistently.

Group VI: Isotransplants After Sensitization and Desensitization of the Donor of the Grafts by Injections of Blood from the Prospective Recipient.—The experiments parallel those of the preceding group with the exception that blood was transferred from the recipients to the donors of the grafts rather than from the donors to the recipients. In other words, the grafts were subjected in their normal habitat to the influence of blood from their future hosts before they were transplanted. In the preceding group the grafts were subjected to no influence before transplantation, but the hosts were prepared in advance of receiving the grafts.

The results in this group likewise paralleled those in the preceding group. Of the 10 grafts from 5 animals which received daily injections for periods of one and two weeks, only 1 survived transplantation, and the epithelial tissue in this instance appeared to be inactive. In this animal and in 3 of the other 4 myxedema developed. Of the 4 grafts from 2 rabbits which received daily injections for four weeks, 1 survived and was definitely hyperplastic. Two grafts could not be found, and 1 had become necrotic and been replaced by fibrous tissue. Myxedema did not develop in either animal.

Group VII: Isotransplants After Sensitization and Desensitization of Both the Donor and the Recipient of the Grafts by Injections of the Donor's Blood to the Recipient and of the Recipient's Blood to the Donor.—In the seventh group of experiments the procedures carried out in the two preceding groups were combined. In other words, not only were the grafts subjected to the influence of blood from their future hosts before they were transplanted, but the hosts likewise were subjected to the influence of blood from the donors of the grafts before receiving them. Twenty rabbits were so treated. Six of them, 3 donors and 3 recipients, received daily injections for one week; an equal number, for two weeks, and 8, 4 donors and 4 recipients, for four weeks. Only 1 of the 20 grafts survived; the donor and the host of this graft had received injections for four weeks. The tissue was definitely hyperplastic, and hypothyroidism did not develop in its host, as it did in 5 of the 10 animals.

Group VIII: Isotransplants After Injections of Nonspecific Blood.—Since, as noted in the foregoing experiments, preliminary injections of specific blood altered the fate of the grafts, the eighth group had for its purpose a test of the influence of nonspecific blood, that is, the influence of small daily and of single massive doses of blood from rabbits which were in no other way related to the experiment. The donor of the grafts neither gave nor received blood. In the 3 animals which received nonspecific blood for one week 3 grafts survived; in

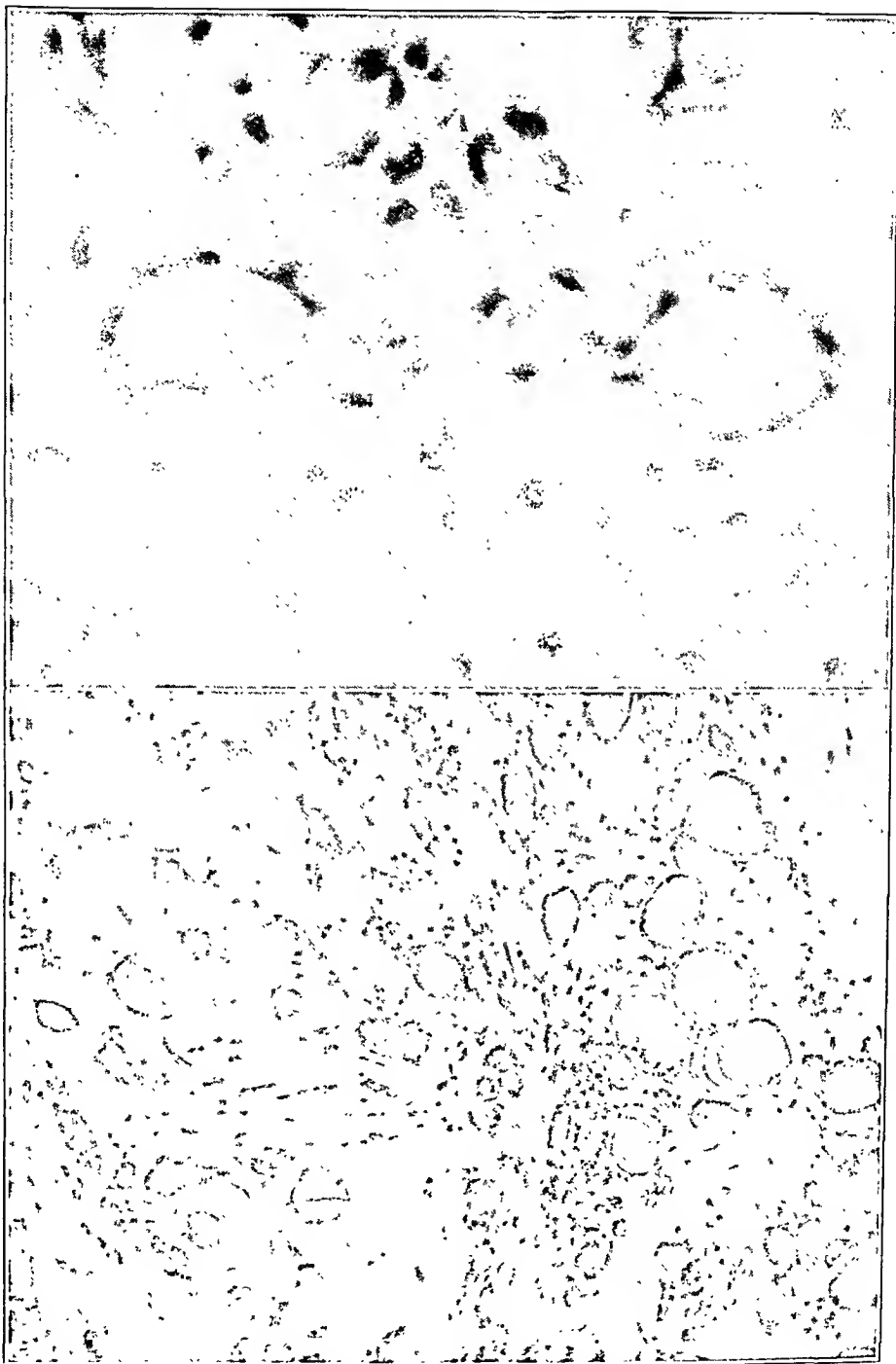


Fig. 4.—Rabbit 88, group VI, isotransplant of one hundred and twenty-one days showing inactive disintegrating thyroid tissue. Only a few follicles lined with flat epithelial cells remain. Most of the tissue has undergone necrosis and has been replaced by fibrous tissue. In this animal myxedema developed, an indication that the transplant was functionally inactive.



Fig. 5.—Rabbit 96, group IX B, necrotic remains of a transplant of human thyroid to a rabbit. The necrotic mass is adherent to the iris. Some ghost follicles remain. Note the inflammatory reaction in both the iris and the transplant. This is probably a reaction to sensitivity.

the 2 which received it for two weeks 2 survived, and in the 2 which received 10 cc. of whole nonspecific blood seven days after transplantation 3 grafts survived and 2 were hyperplastic. No myxedema developed in this group, although no viable grafts were found in 2 of the rabbits. It appears that nonspecific blood exerted little or no influence on the grafts. Fifty-seven per cent of the grafts survived.

Group IX: Transplants of Human Thyroid Tissue to Rabbits.—In many rabbits of the ninth group rather severe reactions of the eyes developed, and many of them died while receiving injections of blood or within six weeks from the time they received the grafts. The results in this group are based on animals which received no injections of blood and on 4 which survived daily injection of blood from the human donors for four weeks. No viable thyroid tissue was found in any of the postmortem specimens, but in most instances there was necrotic tissue accompanied by slight to moderate inflammatory reaction. Only 1 rabbit lived long enough for myxedema to have developed, and it failed to do so.

Group X: Isotransplants After Preliminary Injections of Extracts of the Donor's Tissue.—In the final experiment one lobe of the thyroid gland was removed from each prospective donor of tissue and macerated; a saline extract was then made of it. The entire extract in each instance was proportioned and given in daily intramuscular injections for periods as outlined. At completion of injections the remaining lobe of the thyroid was removed from each donor and transplanted to the respective recipient of the tissue extract. Three rabbits received daily injections for one week, and of the 6 transplants 1 survived and was hyperplastic and 2 necrosed and were replaced by fibrous tissue. In 1 animal myxedema developed. Eight rabbits had daily injections for two weeks, and of the 16 grafts 3 survived and 10 had become necrotic and been replaced by fibrous tissue. The 3 surviving were hyperplastic. In 3 animals signs of myxedema developed. Four rabbits were given daily injections for twenty-two days. Five of the 8 grafts survived and 4 were hyperplastic. Three had undergone necrosis.

These results suggest that, as in the case of specific blood, the tissue extracts sensitized the animals when administered for less than three weeks but failed to do so when given for a period of three weeks or longer.

COMMENT .

It is of interest that an analysis of the results of this investigation shows that transplanted thyroid tissue, though nonviable, delayed the onset of hypothyroidism in totally thyroidectomized animals. As has been stated, it was found in a previous study that in approximately 75 per cent of totally thyroidectomized rabbits signs of thyroid deficiency develop and that these signs appear within eight or ten weeks after expiration of the gland. Of the rabbits which received transplants of thyroid tissue after total thyroidectomy, signs of thyroid deficiency developed, with 1 exception, only in those in which the grafts failed to survive. Signs of hypothyroidism in animals with nonviable grafts, however, appeared not earlier than twelve weeks from the date of thyroidectomy. It would appear, therefore, that the onset of hypothyroidism was delayed by the presence of the grafts despite their failure to survive. Two explanations are possible. Either the grafts

had a temporary take, during which period they functioned, or there was inherent in the tissue and absorbed from it sufficient thyroid principle to delay the onset of signs of deficiency for two or more weeks.

CONCLUSIONS

1. In rabbits heterogenous as well as autogenous grafts not only take in a large percentage of instances but also apparently function.

2. With few exceptions, single massive injections or small daily doses of blood from recipient to donor or vice versa or a combination of both over a period of less than three weeks rendered the recipient or the graft itself sensitive or at least resulted in failure of the graft to take. Although the few exceptions appear to be inconsistencies, they may in reality represent a higher degree of compatibility in those particular animals. If the small daily doses were continued for three weeks or longer, desensitization took place or at least there were takes in a much larger percentage of instances; the percentage was smaller, however, than in the animals which received no blood.

3. Thyroid tissue from dogs transplanted to rabbits failed to survive under any circumstances, including daily doses of blood from the canine donors of the tissue for as long as twenty-five days before transplantations were made.

4. Administration of nonspecific blood, that is, blood taken from a third animal, which was otherwise unrelated to the experiment, did not appear to influence the grafts. The percentage of takes and the condition of the grafts were comparable to those in animals which received no blood.

5. Human grafts in rabbits uniformly failed to survive. Preliminary daily doses of the donor's blood for as long as twenty-eight days seemed not to alter the fate of the transplants. Even the rabbits failed to survive very long. Several died while receiving blood, and the survivors died within a few weeks after receiving the grafts. The eyes of the hosts showed rather marked inflammatory reactions both grossly and microscopically.

6. As in the case of blood, preliminary administration of an extract of a graft for periods of less than three weeks sensitized, and for longer periods desensitized, the recipient or at least altered the percentage of takes accordingly. This effect, however, was less consistent than in animals given blood.

Dr. P. C. Tollman, Assistant Professor of Clinical Pathology, University of Nebraska, examined histologically and gave his opinion on all grafts recovered. Drs. J. M. Ferris and E. L. Boegler assisted with the preparation of the animals and the conduct of the experiment. Miss Mildred Braden prepared the tissue sections for histologic examination.

ATYPICAL CARCINOMA OF THE LARGE INTESTINE

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AND

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The present study was undertaken primarily in order to supply clinical data supported by pathologic findings on the existence of malignant tumors of the large intestine which pursue an atypical course and render clinical diagnosis difficult. The classic syndrome of constipation alternating with diarrhea, blood in the stools, loss of weight and palpable abdominal tumor leads one to suspect carcinoma of the large bowel, but it does not cover the entire situation. By no means do all malignant tumors of the colon present this syndrome. Autopsies repeatedly disclose the fact that many such tumors are symptomatically silent throughout life; on the other hand, they do at times initiate acute symptoms which threaten the life of the patient unless they are accurately diagnosed and prompt, efficient treatment is rendered. The present investigation covers 45 necropsies at which unusual types of carcinoma of the large intestine were observed. The cases reported have been selected from the records of the Jewish Hospital of Brooklyn.

Age and Sex.—The ages of the patients in this series ranged from 28 to 82, averaging 55. The age period of greatest frequency was from 45 to 65 years. In 29 cases, or about 64 per cent of the total number, the lesions occurred in these two decades, and in 40 cases, or about 90 per cent, they occurred between the ages of 39 and 71. These figures are in accord with the records collected from the literature, and they are also in harmony with the general incidence of cancer in any organ of the body. There were 21 males and 24 females, a ratio of approximately 1:1, with a slight preponderance of female patients.

Pathogenesis.—Twelve patients in this series, or 27 per cent of the total number, presented (in addition to carcinoma) single or multiple polypoid growths in the large bowel. The frequency with which polyps appear in the colon is in itself sufficient justification for the prolonged investigations of conditions of that region which might be thought to predispose to carcinoma. It is claimed by many that there exists a direct relation between the presence of polyps and the occurrence of carcinoma of the large bowel. According to Rankin:¹

From the Department of Pathology and Surgery, the Jewish Hospital.

1. Rankin, F. W., and Grimes, A. E.: Diffuse Adenomatosis of the Colon. J. A. M. A. 108:711 (Feb. 27) 1937.

Polyps of the intestine are usually multiple and widely distributed, often extending from the anus to the cecum, but having a tendency to appear approximately eight times more frequently in the rectosigmoid and rectum than in any other section of the colon. This is particularly significant in the light of the similar occurrence and ratio of the distribution of cancer of the colon and immediately suggests a relationship.

The best proof of the association of polyps with carcinoma of the bowel would be the development of carcinoma on a neglected polyp or a polyp which has been kept under observation; this has been reported by numerous observers. Erdmann and Morris² have repeatedly been able in a study of gross specimens in their cases to demonstrate in the same gross specimen all morphologic gradations, from simple polyps, through early infiltrative tendencies, up to frank and unquestioned adenocarcinoma. The practical difficulty, however, lies in the fact that such a lesion when observed is not likely to be left untreated with this possible risk, so that the sequence of events is often difficult to prove. It is likely that when carcinomatous changes do occur the process spreads so rapidly by the inherent penetrative malignancy of the affected cells that it soon blots out any precancerous appearance which might have been present. Allowing for these reservations, it is likely that polyps of the large bowel may be considered the pathologic connecting link between benign neoplasms on the one hand and carcinoma on the other and that it is in the large proportion of cases in which polyps develop that carcinoma is most likely to occur. The practical importance of this does not need stressing. If the physician can identify polypoid changes which are not yet carcinomatous but are likely to proceed in that direction, early removal of the growth will save the patient from the terrors of cancer; this represents prophylactic surgical intervention in the best sense. Unfortunately, however, one is handicapped at the outset by the fact that one may be dealing with a process unapproachable by the ordinary route, so that efficient surgical treatment is hazardous.

It is believed that intestinal irritation resulting from chronic inflammation, such as is seen in cases of chronic colitis, dysentery or tuberculosis, may also be a predisposing factor in the development of carcinoma of the colon. According to Ewing, the transition from simple inflammatory hyperplasia to a tumor which is morphologically, pathologically and clinically adenoma or carcinoma, can clearly be demonstrated. Frequently, a polypoid growth will develop at the site of a chronic inflammation of the colon, and this in turn may eventually give origin to a carcinomatous growth in the bowel. Irritation of the large bowel may also result from prolonged and continuous stagnation

2. Erdmann, J. F., and Morris, J. H.: *Surg., Gynec. & Obst.* 40:460 (April) 1925.

of dried intestinal residue, such as is likely to occur in cases of chronic constipation; this in turn may pave the way in certain cases for development of malignant neoplastic changes of the bowel.

Location and Pathologic Picture.—Table 1 shows the various locations of malignant tumor in our series and needs no special comment except emphasis of the fact that in 26 cases, or 58 per cent of the total number, the rectosigmoid alone was involved.

Furthermore, the occurrence of polyp of the colon was most frequently observed in association with carcinoma of the rectosigmoid, which again emphasizes the close relation probably existing between polypoid growths and carcinoma of the colon. Most of the carcinomas observed in this series were of the cylindric cell type with a tendency toward adenomatous formation. Many of the growths were bulky and cauliflower-like, projecting into the lumen of the intestine on the one hand and on the other infiltrating the depths of the wall. Ulceration and necrosis

TABLE 1.—*Location of Lesion*

Site of Lesion	Total Number	Percentage
Cecum.....	4	9.0
Cecum and ascending colon.....	1	2.2
Cecum and transverse colon.....	1	2.2
Ascending colon.....	3	6.6
Hepatic flexure.....	2	4.4
Transverse colon.....	5	11.1
Splenic flexure.....	3	6.6
Rectosigmoid.....	26	58.0

were common features of such tumors, and in a number of instances the necrosis involved the entire thickness of the wall, resulting in perforation and in the spilling of intestinal contents into the peritoneal cavity. This, in turn, led to the development of either local or generalized peritonitis. It may be of interest in this connection to cite several cases which have been observed in this hospital.

REPORT OF CASES

CASE 1.—The patient was a woman aged 29, who was admitted to the hospital because of acute generalized abdominal pains of one week's duration. She had apparently been in good health prior to this attack. Physical examination at the time of her admission revealed a very sick woman. The abdomen was distended, rigid and tender. A diagnosis of general peritonitis, probably caused by rupture of the appendix was made. At operation the peritoneal cavity was found to be filled with purulent material, and consequently no attempt was made to ascertain the primary site of the lesion. The peritoneal cavity was drained, but the patient died shortly afterward. At necropsy the peritoneal cavity was observed to be filled with pus. The sigmoid flexure was the seat of a large, ulcerative cauliflower-like mass with a large central perforation through which seepage of intestinal contents took place into the free peritoneal cavity. Microscopic examination of the tumor proved it to be an adenocarcinoma.

CASE 2.—A man aged 58 was admitted to the hospital because of acute abdominal pains of two days' duration. Except for constipation, with which he had been troubled for the past two years, the patient had enjoyed good health until the onset of the present illness. On admission to the hospital he was acutely ill, and the abdomen was distended and tense. A diagnosis of acute intestinal obstruction was made, but he died before surgical intervention could be undertaken. At necropsy a perforated, ulcerative growth of the sigmoid was observed, together with generalized peritonitis. In addition to the carcinoma, multiple polyps were present in the small and large intestines. There was no evidence of metastasis. Histologically the tumor of the sigmoid was found to be an adenocarcinoma.

CASE 3.—The patient, a man aged 49, was admitted to the hospital because of abdominal pains and vomiting of three days' duration. Prior to the onset of the present illness he had had comparatively good health. A few days previously he had noticed abdominal distention, constipation and obstipation. None of the symptoms was relieved by cathartics or enemas. At operation a perforated carcinoma of the sigmoid was found. The patient died soon after operation, and at autopsy generalized peritonitis was observed, resulting from a perforated carcinoma of the sigmoid. No metastasis was observed.

CASE 4.—A 55 year old woman was admitted to the hospital because of acute abdominal pains and vomiting of one day's duration. For nine or ten months prior to admission she had had episodes of constipation alternating with diarrhea, but no other symptom referable to the intestinal tract had been noticed. On examination she appeared acutely ill and presented a large mass in the pelvis, which was thought to be an ovarian cyst with a twisted pedicle. At operation the mass felt in the pelvis proved to be an encapsulated collection of pus, and this was drained. The patient soon succumbed, however, to infection, and at autopsy a perforated carcinoma of the sigmoid was observed. Localized pelvic peritonitis was present. Microscopic examination of the tumor showed it to be an adenocarcinoma. There was no evidence of metastasis anywhere in the body.

These cases illustrate the almost complete lack of symptoms presented by carcinoma of the large intestine and the acute, fulminating course which such a lesion may follow. It is also of interest to note that none of the patients in this series showed any evidence of metastasis, and we attribute this primarily to the acuteness of the lesion, which caused death long before metastasis could develop.

In certain rare instances portions of the growth may slough away completely and give rise to severe hemorrhage. In such cases, also, the broken-off tissue may be expelled through the rectum; the tissue thus recovered may be subjected to pathologic examination and the nature of the lesion determined. This occurred with 1 of our patients, a woman aged 71, who suddenly had a profuse intestinal hemorrhage and expelled, in addition to the blood and blood clot, a large mass of partly necrotic tissue. Histologic examination of the expelled specimen proved it to be an adenocarcinoma of intestinal origin.

Perforation of a carcinomatous intestine does not always take place into the free peritoneal cavity; it may take place into an adjoining viscus and then establish a fistulous communication between the per-

forated bowel and the involved viscus. Several such instances occurred in our series, some of which will be cited as examples.

CASE 5.—A 59 year old man was admitted to the hospital because of pain, nausea, vomiting and extreme weakness. He died within a short period, and at autopsy two separate carcinomatous growths were observed, one in the cecum and the other in the transverse colon. The carcinoma in the cecum had perforated into the stomach, producing a fistulous communication between these two organs.

CASE 6.—The patient was a man aged 44, who for ten days prior to his admission to the hospital had been complaining of abdominal pains, nausea, vomiting and weakness. He had episodes of rectal bleeding at varying intervals. On examination the patient appeared acutely ill; the abdomen was tense and transmitted a sense of fulness to the examining hand. He died within a short period after entering the hospital, and at autopsy a carcinoma of the splenic flexure was observed. It had perforated into the stomach, producing a gastrocolic fistula. Widespread metastases to the liver, the spleen and the thoracic duct were observed, together with diffuse chylous peritonitis; the latter condition was due to obstruction of the thoracic duct by tumor tissue.

CASE 7.—Perhaps one of the most interesting cases of this group is the following: A man aged 54 was admitted to the hospital with a complaint of cutting, burning and pressing pains in the pelvis; these pains were aggravated on urination. The symptoms had been present for four months. The patient had been apparently well until six months prior to admission, when he strained considerably at stool and passed a small amount of feces stained with blood. The blood continued to appear in the stools for one week and then stopped. During the next two months he remained well except for constipation, for the relief of which he had to use a considerable amount of liquid petrolatum and castor oil. Four months prior to admission he was suddenly seized with a cutting and burning pain along the penile portion of the urethra; this pain was much worse on urination. He had considerable difficulty in starting the urinary flow, and he began to note for the first time the passage of blood and fecal matter in the urine.

On examination at the time of admission the patient was well developed and fairly well nourished and did not appear acutely ill. The abdomen was scaphoid and soft; a sausage-shaped tumor was palpable in the left lower abdominal quadrant. Rectal examination showed the vesical wall thickened and indurated, and a soft mass could be felt between the bladder and the anterior wall of the rectum. A cystogram showed a free communication between the posterior aspect of the bladder and the anterior surface of the sigmoid. A sigmoidoscopic examination proved entirely unsatisfactory. Cytoscopic examination showed intense generalized cystitis in addition to a large tumor, irregular in outline, situated at an area covering the left lateral wall, the posterior wall and the roof of the bladder. The top surface of the vesical tumor showed some degree of necrosis. Surgical intervention was felt advisable, and at operation the sigmoid flexure was removed together with the bladder, in one mass. The patient, however, failed to recover from the operation and died soon afterward. Pathologic examination of the specimen revealed an ulcerating carcinomatous growth of the sigmoid flexure, which had perforated into the bladder, producing a fistulous tract between the two organs. A secondary metastatic growth was observed, involving the posterior wall of the bladder. Microscopic examination of tumor tissue recovered from both the bladder and the sigmoid flexure showed it to be an adenocarcinoma of intestinal origin.

CASE 8.—Another case, somewhat similar to case 7, is the following: A 52 year old woman had progressive dysuria for four months. She did not complain of symptoms referable to the intestinal tract. On admission to the hospital she appeared well developed and rather obese. There was tenderness in both flanks and in the suprapubic region. Rectal and vaginal examinations gave negative results. The urine gave a 3 plus reaction to the test for albumin. The sugar content of the urine was 1.5 per cent, and clumps of pus and numerous red blood cells were present. The blood count showed: hemoglobin, 90 per cent; erythrocytes, 4,500,000; leukocytes, 9,900, and polymorphonuclears, 80 per cent. The sedimentation rate of the blood was 80 mm. in one hour. The reaction of the stools to the guaiac test was negative. There was 20 cc. of residual urine in the bladder. Culture of the urine showed *Bacillus coli*; the phenolsulfonphthalein test showed excretion of 69 per cent in two hours. Cystoscopic examination revealed marked cystitis in addition to a large globular mass occupying the right upper vault of the bladder. A biopsy of material from the mass was done, and the pathologic findings were those of an adenocarcinoma, probably of intestinal origin. A cystogram and aerogram showed a large filling defect in the vault of the bladder. At operation a large encircling carcinoma of the sigmoid flexure was found; it had invaded the bladder and the surrounding structures by direct continuity, forming a large frozen and inoperable pelvic mass. There were also a few metastatic nodules in the liver.

This case illustrates the complete lack of symptoms of the primary lesion in the sigmoid flexure in spite of its extensive growth and widespread metastasis. Cytologic examination of a biopsy specimen removed from the tumor in the bladder revealed the fact that the primary site of the growth was in the large intestine and that the tumor in the bladder was secondary.

The other type of tumor frequently encountered in this series was the annular or constricting form. This did not, as a rule, present a bulky mass of tissue growing into the lumen of the intestine, but it infiltrated the depth of the wall, replacing the various intestinal coats. The patients with this type of growth often succumbed rather suddenly to acute intestinal obstruction, which at autopsy proved to have been caused by an adenocarcinomatous stricture of the large intestine. A few such cases will be cited as examples.

CASE 9.—A 28 year old woman was admitted to the hospital with a history of an acute onset of abdominal pains, vomiting and obstipation of thirty-six hours' duration. She was apparently well until three months prior to admission to the hospital, when she first had diarrhea. The condition lasted one week and then subsided. She remained well until the present attack of abdominal pains and vomiting, thirty-six hours before her admission to the hospital. On admission the patient appeared acutely ill; the abdomen was distended, and she was vomiting stercoral material. Her poor general condition did not permit surgical intervention, and she died twenty-four hours later. At autopsy a constricting tumor of the sigmoid was observed, which microscopically proved to be an adenocarcinoma. Numerous polyps of the large intestine were also observed. There were no metastases.

CASE 10.—A man aged 82 was apparently well until four weeks prior to his admission to the hospital, when he began to complain of loss of appetite, loss of weight and vomiting. Two weeks before his admission the stools were loose and black. On examination no abnormality was noticed; the pains and vomiting

soon subsided, and the patient was discharged. He was readmitted seventeen days later because of intermittent gnawing pains in the abdomen. The abdomen was tense and much distended. The patient died two hours after entering the hospital. At autopsy a carcinomatous stricture of the sigmoid flexure was observed. Diffuse peritonitis was also present. There were no metastases.

CASE 11.—A 57 year old woman was admitted to the hospital complaining of nausea and vomiting after meals, sticking pains in the abdomen, borborygmi and constipation. The symptoms had appeared four weeks previously. She had been constipated for a number of years, but in the past four weeks the constipation had become obstinate and had not responded to cathartics or enemas, except to high colonic irrigations. On examination at the time of admission, the abdomen was distended and tympanitic. No masses could be palpated either abdominally or rectally. The patient was operated on for intestinal obstruction, but she succumbed to the operation. At autopsy a constricting adenocarcinoma of the sigmoid was observed.

CASE 12.—The following case is of particular interest: A woman aged 50 was admitted to the hospital because of abdominal cramps and vomiting. She had been in good health until two months prior to admission, when she first noticed slight epigastric distress, which was relieved by sodium bicarbonate. Two weeks later she was seized with severe abdominal cramps associated with vomiting and retching, which subsided after she took an enema. Since then she had had repeated mild seizures of intestinal cramps associated with constipation alternating with diarrhea. There was no blood in the stools. Seven days before entering the hospital she was again seized with excruciating general abdominal pains, and at this time enemas failed to relieve her. Two days later she began to vomit, and she continued to do so at least once daily. She had had no evacuation of the bowels for the last seven days, in spite of the many enemas which she had received.

On admission to the hospital the patient appeared well developed and well nourished but acutely ill and in great distress. The facies was somewhat cyanotic, and the skin was cold and clammy and covered with beads of perspiration. The abdomen was distended and spastic. A questionable mass was palpable in the left upper quadrant of the abdomen, which was firm but not tender. The preoperative diagnosis was acute intestinal obstruction, probably caused by a malignant growth. At operation, a constricting growth encircling practically the entire circumference of the sigmoid flexure was discovered. The sigmoid was resected, and pathologic examination of the specimen revealed an adenocarcinomatous stricture of the sigmoid. The inner surface of the growth adjoining the lumen of the intestine was ulcerated, and lodged within the ulcer was a vertebra of a squab, which caused complete obstruction of the intestine at this point.

COMMENT

In the 45 cases in which necropsy was done the liver was by far the most frequent site of metastasis, with the regional lymph nodes next, and direct infiltration of the peritoneum, the omentum and the adjoining organs last.

Table 2 shows the sites of metastasis in the 45 cases and demonstrates the relatively large percentage of cases in which metastasis occurred. The high proportion of cases in which the liver was involved, almost twice the proportion in which the regional lymph nodes were involved,

leads one to assume that the hepatic spread must be blood borne. Furthermore, of the 16 carcinomas from which metastasis occurred, 11 originated in the rectosigmoid; 8 of these metastasized to the liver. The infrequency of peritoneal seeding in this disease (2 cases) as compared with its frequency in other intra-abdominal malignant diseases is remarkable. Obstruction of the thoracic duct by carcinomatous tissue in 1 of the cases is of interest and explains the development of the chylous peritonitis that was noted. The presence of two independent carcinomatous lesions in two different organs of the body is also of great interest. One of the patients showed at autopsy a bronchogenic carcinoma in addition to carcinoma of the cecum. Clinically the symptoms presented by this patient pointed to a carcinoma of the lungs; he had no symptoms that pointed to a tumor of the cecum, and the finding at autopsy of a carcinoma of the cecum as well as a bronchogenic carcinoma was rather surprising.

TABLE 2.—*Sites of Metastasis*

Metastasis	Total	Percentage
Total cases.....	16	35.5
Liver.....	10	62.5
Regional nodes.....	6	37.5
Peritoneum.....	2	12.5
Omentum.....	1	6.2
Ovary.....	1	6.2
Diaphragm.....	1	6.2
Lungs.....	1	6.2
Kidney and pancreas.....	1	6.2
Spleen and thoracic duct.....	1	6.2

In another case a diagnosis of carcinoma of the ovary was rendered, but at autopsy, in addition to a carcinoma of the ascending colon, a carcinoma of the ovary was observed, cytologic examination of which proved it to be adenocarcinoma of different cell origin.

Perhaps one of the most unusual cases in our series was that of a patient in whom carcinoma of the rectum developed while he was under treatment for lead poisoning. This case has already been reported by Gray and Greenfield³ from this hospital. The following is a brief summary: A man aged 51 was exposed to the inhalation of lead fumes in an enclosed chamber and later had abdominal colic associated with weakness, anorexia and constipation. Because of the progressiveness of the symptoms he had to stop work five months after having been first exposed to the lead fumes. Physical examination revealed marked pallor but no other unusual finding. The blood showed a moderate degree of anemia and stippling of the red blood cells. All other laboratory examinations were reported as giving negative results. Delead-

3. Gray, I., and Greenfield, I.: New York State J. Med. 37:649 (April 1) 1937.

ing therapy was instituted, and the patient began to excrete lead in the stools and in the urine. The abdominal colic disappeared, and the function of the bowel returned to normal. Four months after cessation of exposure to lead, profuse rectal bleeding occurred. Rectal examination revealed a hard, irregular mass occupying the anterior wall of the rectum, just above the prostate. The patient was operated on for excision of the tumor, but he succumbed to the operation three weeks later. Pathologic examination of the specimen obtained from the rectum proved it to be an adenocarcinoma.

A search through the literature reveals numerous descriptions of the symptoms of carcinoma of the colon, but the difficulty is that they usually have no application to the particular case. It is emphasized that many carcinomatous lesions of the colon mimic other intra-abdominal conditions and offer no evidence of an existing intestinal lesion. This is particularly true of the acute, fulminating forms of malignant tumor, which often advance to perforation or obstruction before the true nature of the lesion can be discovered.

It is still a general belief that carcinoma of the colon is often associated with constipation and diarrhea and that these symptoms are rather pathognomonic of the lesion. An analysis of the various symptoms presented by this group of patients with carcinoma of the colon shows that constipation and diarrhea, which were noted in 27 and 9 cases respectively, were probably no more frequent among our patients, than they are among presumably normal persons of the same age. Diarrhea was less common than constipation and probably has no value as a diagnostic sign. The simultaneous occurrence of diarrhea and constipation was even less frequent; it occurred in only 5 cases of the series. Pain was a frequent complaint and occurred in 42 cases, but considering the fact that in most cases the condition ran a very acute course and was frequently complicated by intestinal obstruction and peritonitis, such pain cannot be regarded much longer as symptomatic of carcinoma of the colon. Nausea and vomiting occurred in 17 cases; in 11 of these, autopsy revealed a carcinomatous stricture with intestinal obstruction or a carcinomatous perforation of the bowel with peritonitis. Undoubtedly, the nausea and vomiting were caused rather by the peritonitis or intestinal obstruction than by the tumor per se, as in 28 cases in which no complicating factors were present there was no nausea or vomiting. Only 15 patients, or one third of the total number, presented a palpable mass in the abdomen on either rectal or abdominal examination. In some cases the palpated mass was tender, while in others it was painless. The presence of blood in the stools was noted in 11 cases. In 2 instances the bleeding was profuse, and in another it was associated with the expulsion of a mass of tumor tissue, largely necrotic. In 1 case bleeding appeared through the urethra because of a sigmoidovesical

fistula. In 2 the blood was mixed with mucus, and in 3 it was black and was recorded as melena. In 20 cases there was no history of loss of weight; in 1 the loss of weight was reported as amounting to 80 pounds (36.3 Kg.), while in several cases it averaged 20 pounds (9.1 Kg.). On the whole, loss of weight was not a striking feature. Weakness was noted in 25 cases, but this, again, might have been due to the acuity of the lesion and the complicating factors that were noted in so many of our reported cases. In about half the cases the patients were well developed and well nourished and appeared fairly healthy.

The duration of symptoms referable to the intestinal tract was variable in the different cases studied. Many patients had vague symptoms suggestive of intestinal disturbance which extended over two years and more but which terminated in an acute episode lasting for periods varying from a few hours to several days. The average duration of symptoms before the patient sought the advice of a physician was about six months. Our data are not sufficiently detailed to permit conclusions as to the roentgenologic or proctoscopic findings in cases of malignant tumor of the large intestine. Many of the patients were acutely ill on entering the hospital, and roentgenologic or proctoscopic examination was inadvisable. Therefore, no consideration of such accessory aids in the diagnosis of carcinoma of the colon was undertaken in this series of cases. Allowing for such reservations, it may be said that patients with a palpable tumor, loss of weight, bleeding from the rectum and signs of intestinal obstruction or perforation probably were all at the stage at which nothing could be done to help them. The disease was far advanced before they had any reason to suspect its existence.

SUMMARY AND CONCLUSIONS

Forty-five cases of atypical carcinoma of the large bowel, with autopsic observations, are reported. The symptoms presented by most of the patients were indistinguishable from those of other acute intra-abdominal conditions and rendered clinical diagnosis very difficult.

Among the cases reported in this series, perforation and obstruction of the carcinomatous bowel were commonly observed. In 1 case the obstruction was caused by a foreign body lodging in the sigmoid at the site of the growth. In 2 cases the tumor invaded the urinary bladder and gave rise to urinary symptoms alone, but biopsy of material from the tumor in the bladder proved it to be of intestinal origin. In 1 case carcinoma of the colon was associated with a bronchogenic carcinoma, in 1 with an ovarian carcinoma and in 1 with lead poisoning.

In 27 per cent of cases the tumor in the bowel was associated with a polypoid growth in the intestine.

The symptoms of carcinoma of the large intestine are readily confused with those of other intra-abdominal conditions.

OVARIAN TUMORS AND DIAGNOSIS OF ACUTE APPENDICITIS

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An analysis of a large group of cases of ovarian tumor (1,101 cases) disclosed that 103 laparotomies were performed after a diagnosis of acute or chronic appendicitis had been made. That disease of the ovary may simulate appendicitis, disturbances of the gallbladder or genitourinary tract, ectopic gestation and other abdominal or pelvic conditions is well known. Generally the symptoms of an ovarian growth differ sufficiently from those of appendicitis to warrant careful differentiation before radical treatment is instituted. The salient features of ovarian tumor and the clinical and operative findings as here disclosed may serve to indicate the causes of the high incidence of diagnostic error.

Physicians often examine a normally menstruating, unmarried young woman to determine the cause of pain in the lower part of the abdomen. I have found that the incidence of ovarian pathologic change in such patients is especially high.

Sixty-three patients (61 per cent) were under 20 years of age; 37 (36 per cent) were between 20 and 30, and only 3 (3 per cent) were over 40. Most of them were single (64 per cent). Although ovarian structure was altered in all the cases, menses were normal in 83 per cent. In 11 per cent of cases there was metrorrhagia; in 5 per cent there was secondary amenorrhea; and in 1 per cent there was primary amenorrhea. Although dysmenorrhea occurred in 25 per cent of the patients, this symptom was predominant only among patients under 20 years of age.

The syndrome of recurrent severe or mild interval pain (*Mittelschmerz*) is commonly found in the histories of such patients. The intermenstrual incidence, periodic recurrence and short duration of the pain are significantly constant. It was interesting to note that 70 per cent of the patients in this series had histories of repeated attacks of pain in the lower part of the abdomen, which always occurred during the menstrual interval. More than half the patients had had over five attacks. In several instances the attacks dated back to the onset of the menses; other instances of interval pain for three to five years are reported, but the majority (80 per cent) had noticed repeated pain in the lower part of the abdomen for only four to ten months. Twelve patients were operated on at the time of the first attack.

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The severe onset persisted usually for six to twelve hours but subsided into a low grade pain which disappeared gradually in one week. Several instances of continuous, annoying interval pains terminating in intolerable dysmenorrhea were also noted. There were also single instances of spontaneous colicky pain occurring for the first time, which nothing but morphine could relieve. Although nausea and vomiting were frequent, the patients did not abstain from eating.

Since involvement of the right ovary brings up the question of appendicitis, the following findings are noteworthy. Structural changes in the right ovaries of 82 per cent of these women were noted. In 10 patients the left ovary was involved, and in 7 both ovaries showed changes; disease of the appendix was found in only 4 cases.

The rare phenomenon of unilateral pain produced by diseased tissue of the contralateral side is well known. This analysis indicates, however, that with regard to the ovary the phenomenon is not as rare as is commonly supposed. In 20 per cent of the patients the site of the pain was contralateral to the affected ovary. However, in most of the patients (68 per cent) who complained of pain on the right side with or without pain in other areas the right ovary alone was involved; and in several instances bilateral ovarian disease was found. Not always does bilateral pain in the lower quadrants of the abdomen manifest bilateral ovarian disturbance; in 9 instances a tumor of the right side of the pelvis and in 2 instances a tumor of the left side of the pelvis was the site of origin of bilateral pain. Only in 1 instance, however, was disease of the ovary bilateral.

Although all the histories indicated that the clinical onset in both acute and chronic conditions was sufficiently severe to warrant operation for appendicitis, the operative findings revealed a striking absence of appendiceal disease in all but 7 patients.

The findings are derived from two groups, namely those patients for whom chronic attacks of appendicitis were reported and those in whom the onset was severe enough to be classified as acute appendicitis. There were 45 patients with chronic appendicitis; for these patients the findings were as follows: One patient had ovarian endometriosis and tuberculous adnexitis; 1 had an endometrial cyst of the ovary; 25 had follicular cysts, none of which showed rupture; 9 had corpus luteum cysts; 8 had polycystic ovaries, and 1 had a hydrosalpinx on the right side with a simple ovarian cyst (this patient also had a carcinoid of the appendix).

In this group only 1 instance of an appendiceal lesion was found; in the same patient, however, a hydrosalpinx on the right side and a simple ovarian cyst were sufficient to cause the symptoms. Thus, except for the 2 cases of endometriosis, simple cyclic ovarian changes such

as follicular and corpus luteum cysts produced symptoms of chronic appendicitis.

There were 58 patients for whom a diagnosis of acute appendicitis was made and the onset characterized as severe. All lesions found in this group were related to the ovary, but 6 appendical lesions were also found. Two of these, namely, foreign body and oxyuriasis of the appendix, were accompanied by ovarian torsion, which, it may be fairly assumed, produced the acute symptoms. Appendical lesions with suppuration or gangrene undoubtedly accounted for the symptoms of the remaining 4 patients, even though ovarian pathologic change was also present.

The following lesions were found at operation: 37 follicular cysts, 12 ruptured and 1 gangrenous (there were 3 suppurative appendixes in this group); 9 corpus luteum cysts, 5 of which showed rupture; 9 dermoid cysts, 4 with torsion (there was 1 gangrenous appendix in this group); 1 bilateral microcystic ovary (the patient was psychoneurotic); 1 parovarian cyst, and 1 instance of ovarian endometriosis of the ovary with uterine pregnancy.

Thus, for these 58 patients operated on for acute appendicitis only 4 appendical lesions were found severe enough to warrant such a diagnosis. Not even all the ovarian changes, although present throughout, were sufficient to produce symptoms indicating immediate surgical intervention. Ordinarily a simple follicular or corpus luteum cyst is not of surgical significance, and it is noted also that two thirds of the follicular cysts and half of the corpus luteum cysts were unruptured. Microcystic ovaries, although occurring in a psychoneurotic patient, generally do not simulate acute appendicitis. The dermoid, parovarian and endometrial cysts, however, all indicated operation.

SUMMARY

1. In 45 patients whose condition was diagnosed as chronic appendicitis no pathologic change was found in the appendix to warrant this diagnosis.

2. In 58 patients whose condition was diagnosed as acute appendicitis, only 4 appendical lesions were found indicating operation.

3. About 32 per cent of all ovarian lesions were severe enough to account for the appendicitis syndrome. (These included ruptured follicle cysts, endometriosis, dermoids and torsion.)

4. Eighty-nine per cent of the ovarian changes were purely cyclic or functional (follicular cysts, microcysts and corpus luteum cysts) conditions ordinarily requiring no operation; 26 per cent of these, however, were ruptured.

5. Twenty-three per cent of patients whose condition was diagnosed as appendicitis were found to have acute onset of pain, caused by torsion, by rupture, by gangrene or by an ovarian tumor (all types).

6. Ovarian disease accounted for 96 per cent of abnormal operative findings. Appendical disease represented only 4 per cent. Thus, the appendix was a direct cause of the syndrome diagnosed as appendicitis in only 4 per cent of patients in this group; a 96 per cent error was made in diagnosis.

7. Operative findings warranting surgical intervention aggregated 14 per cent. (These included appendical and ovarian pathologic conditions, such as dermoid, endometriosis, hydrosalpinx and tuberculous adnexitis.)

8. The high incidence of unmarried patients (64 per cent) and normal menstrual histories (83 per cent) as well as the incidence of dysmenorrhea (25 per cent) is of interest.

Significant as causes for diagnostic error are the 20 per cent frequency of pain which occurred contralaterally to the site of disease and the 78 per cent incidence of involvement of the right ovary which produced pain in the right lower quadrant of the abdomen, similar to that of appendicitis.

The youth of the patients (88 per cent under 30 years of age) and the repeated attacks of interval pain (*Mittelschmerz*) in 70 per cent, as well as the rapidly subsiding symptoms, are sufficient reasons for proceeding slowly before operation is undertaken in such cases.

The symptom of acute pain in the right lower quadrant of the abdomen in an unmarried female patient under 30 years of age may closely simulate appendicitis, but a painstaking history and a twenty-four hour period of careful observation will in many instances spare the patient an unnecessary operation.

A NEW SURGICAL MASK

A BACTERIOLOGIC AIR FILTER

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There is ample evidence in recent surgical literature to show that surgeons are not satisfied with the present methods of face masking. Walker¹ in 1930 outlined what he considered the requirements of an ideal mask and hastened to state that he had not yet found it. Waters² in 1936 pointed out that improper surgical masking has constituted a persistently weak link in the chain of aseptic operative technic. Walker in 1935 presented bacteriologic evidence as to the source of hemolytic streptococci in four epidemics in hospitals, three in surgical services and one in an obstetric service. Cultures of material taken from hands, instruments, solutions and sterile goods at the time of these epidemics failed to show hemolytic streptococci. The masks were found to be ineffective and half of the operating room personnel were found to be carriers of hemolytic streptococci. Meleney³ in 1935 studied the bacterial flora of the air in his operating rooms and estimated that from 35,000 to 60,000 bacteria fall on the sterile operative field during the course of one hour. Davis⁴ in 1937 stated:

In short, I feel that adequate masking is not only essential but is the most important, in addition to rubber gloves and gentle handling of tissues, that the surgeon can personally carry out to prevent infection in clean operative wounds.

Blatt and Dale⁵ in 1933 advocated the use of impermeable deflector masks. These are not filters. Waters in 1936 described a similar impervious deflector mask.

From the Department of Bacteriology and Public Health, the University of Illinois College of Medicine.

1. Walker, I. J.: How Can We Determine the Efficiency of Surgical Masks? *Surg., Gynec. & Obst.* 50:266, 1930.

2. Waters, E. G.: Adequate Surgical Masking: Problem and Solution, *Am. J. Surg.* 32:474, 1936.

3. Meleney, F. L.: Infection in Clean Operative Wounds, *Surg., Gynec. & Obst.* 60:264, 1935.

4. Davis, J. S.: Is Adequate Masking Essential for the Patient's Protection? *Ann. Surg.* 105:990, 1937.

5. Blatt, M. L., and Dale, M. L.: A Bacteriological Study of the Efficiency of Face Masks, *Surg., Gynec. & Obst.* 57:363, 1933.

Gardner, Hart and Durham⁶ in 1937 ably and comprehensively reviewed the recent literature in regard to advances in surgery from a bacteriologic point of view.

Eight years ago I had occasion to study the relative effectiveness of textiles as to their power to absorb bacteria. Among the materials used were silk, linen, cotton and wood cellulose in the form of a creped wadding called cellucotton. These materials were teased out into single fibers; the fibers were submerged in suspensions of bacteria and then were removed and washed three times. Centrifugation was used between washings to recover the fibers, which were then fixed on slides and stained. Figure 1 is a photomicrograph of cellucotton, cotton and linen treated in this manner. Staphylococcus aureus was the organism used. Figure 2 is a high power photomicrograph of the cellucotton fibers showing the staphylococci on the topmost fiber.

A member of the surgical staff came to me several months ago for help and suggestions as to the problem of reducing the hazards of transmitting in operating rooms the bacterial flora of the upper part of the respiratory tract. We have studied this from two standpoints; first, the temporary reduction (for a period of two hours) of bacterial flora in the mouths and throats of the operating room personnel, and second, the investigation of masks to filter out the expelled flora. The latter subject will be reported in this paper. The first problem is still being studied. We have, however, some encouraging results, and we hope to be able to report something of practical value within a few months.

We were not concerned with deflecting bacteria from the operative field but desired to filter out the bacteria from the expired air. Our work has been made possible by the use of the air centrifuge of Wells.⁷ This useful apparatus allows the investigator to count the bacteria per unit of air in a manner similar to that in which one counts bacteria per unit of any fluid, such as water or milk. We could not have carried out these studies if we had used the old open Petri dish method for bacterial counts. I do not desire to take up space describing this useful apparatus. The quantity of air to be analyzed is pulled into this machine by a suction fan, and the bacteria are deposited by centrifugal power on the surface of a glass cylinder coated with the desired agar medium, plain agar, blood agar or chocolate agar. The size of the particles and are at the bottom of the cylinder. The heavier particles settle first containing the bacteria, such as droplets of expelled exudate or saliva.

6. Gardner, C.; Hart, D., and Durham, N. C.: Recent Advances in Surgery from a Bacteriologic Viewpoint, *Surgery* 1:458, 1937.

7. Wells, W. F.: On Air-Borne Infection: II. Droplets and Droplet Nuclei, *Am. J. Hyg.* 20:611, 1934.

can be accurately determined by a reading of the results after incubation of this cylindric tube coated with a culture medium. The heavy particles are on the bottom; the bacteria, free of accompanying pus and mucus, are toward the upper end of the tube. We are using this apparatus for various purposes associated with routine surgical and obstetric service. The instrument and the technic yield exact information relative to many environmental conditions which have been considered in the past but owing to lack of accurate technical methods have been more theoretic than practical.



Fig. 1.—Photomicrograph of cellulose, cotton and linen fibers. The upper two larger fibers are cellulose. The uppermost fiber has been in contact with a suspension of bacteria and has been washed three times. Note the large number of bacteria still adhering to the fiber. The next large fiber is of clean untreated cellulose. The middle two fibers are cotton; the upper one of these two was treated the same as the top cellulose fiber. There are few bacteria remaining on this fiber. The fourth fiber from the top is a control, an untreated cotton fiber. The lower two fibers are linen. The bottom fiber is the control; the fiber above it has been in contact with bacteria the same as the topmost cellulose fiber. Few bacteria can be observed on this linen fiber.

Hart⁸ in 1937 recommended sterilization of the air in operating rooms by bactericidal radiant energy. This is another approach to the

8. Hart, D.: Sterilization of the Air in the Operating Room by Bactericidal Radiant Energy, *Surgery* 1:770, 1937.

problem of controlling the transmission of flora of the upper part of the respiratory tract in surgical procedures. The reports so far of the use of this method seem encouraging, but it is still experimental and has not been accurately standardized. The recirculated and incoming

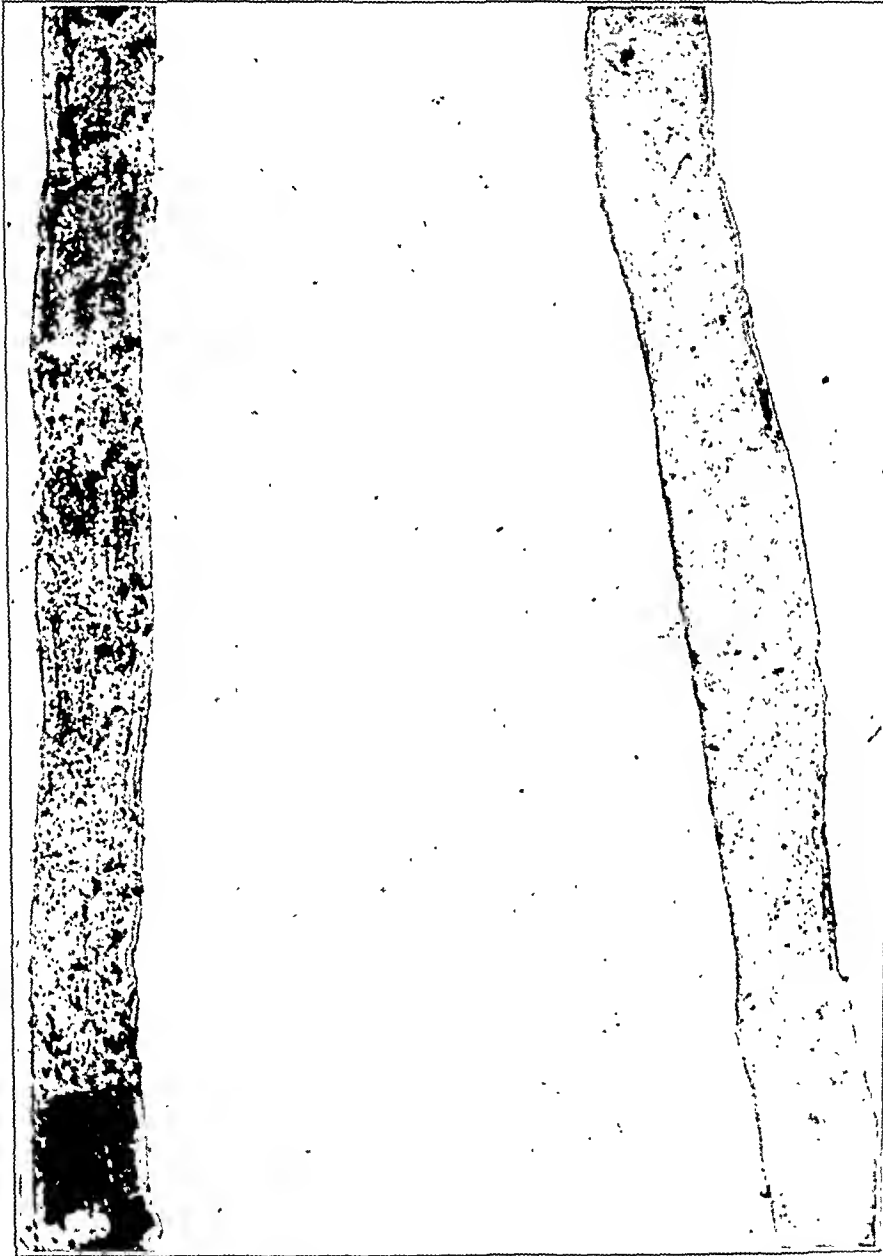


Fig. 2.—Photomicrograph of cellulose fibers from cellucotton. The single fiber on the left has been exposed to bacterial suspension and washed three times. The fiber at the right is a control. It is an untreated, fresh fiber.

air could be passed through a cellulose filter, the personnel being masked with these bacterial absorbent materials. As a safeguard for dissemination by air of oral and nasal bacterial flora from unmasked observers and visitors, radiant energy might be used to destroy the residual bacteria in the atmosphere. It seems to us a sounder procedure to prevent contamination of air and to control as well as to restrict the distribution of bacteria in the atmosphere of the operating room by bacteriologic filtration than to allow gross pollution to occur and depend on radiant energy to make the air safe for all concerned. Bactericidal radiant energy has its uses, but like chlorination of water or pasteuriza-

TABLE 1.—*Effect of the Number of Plies of Cellucotton on Its Efficiency as a Filter**

Room air control.....	182 colonies
2 ply cellucotton.....	6 colonies
3 ply cellucotton.....	4 colonies
4 ply cellucotton.....	3 colonies
5 ply cellucotton.....	1 colony (spreader)
6 ply cellucotton.....	0

* The number of bacteria are expressed per 10 cubic feet of air. An average of 33 experiments was performed with each type of filter.

TABLE 2.—*Influence of the Number of Plies of Cotton Gauze on the Efficiency of the Bacterial Filter**

Room air control.....	164 colonies
2 ply gauze.....	31 colonies
4 ply gauze.....	24 colonies
6 ply gauze.....	15 colonies
8 ply gauze.....	9 colonies

* The number of bacteria are expressed per 10 cubic feet of air. An average of 16 experiments was performed with each type of filter.

tion of milk it is most useful when employed in conjunction with and in augmentation of other standard sanitary procedures for purification of air.

We attached a large glass funnel to the intake tube of the Wells air centrifuge. Our experiments were divided into two parts, the studies in filtration of air and the application of these results to the improvement of surgical masks.

In all, 94 experiments were conducted in the air filtration studies. The principle was to cover the 6 inch (15 cm.) funnel at the intake of the Wells air centrifuge with the material to be tested. We were able to seal the funnel so that all of the air passed through the filter. Face masks cannot be controlled in this manner. There is always leakage around the masks, usually above.

Table 1 gives the results of the use of cellucotton filters for the air going into the air centrifuge. Table 2 gives the results obtained when gauze filters were used in the same way. The cotton gauze offers

greater resistance to the passage of air, but in this experiment the air had to filter through the cellucotton or gauze. The suction of the machine and the tightly fitting layers of the material forced the air to pass through the filters. When gauze is used for a face mask the escape of the expired air above the mask is more noticeable than when cellucotton is used. The line of least resistance is upward on each side of the nose when four or more thicknesses of gauze are used for a face mask.

We have not found a method of testing the efficiency of masks to remove bacteria from the expired air. We have determined the average bacterial count per unit volume of air in the room. The masked person talked while his face was directly in front of the large glass funnel attached to the intake part of the air centrifuge. Room air naturally

TABLE 3.—*Bacterial Counts per Ten Cubic Feet of Air**

Room air control.....	295
Without mask.....	720
8 ply ordinary gauze mask.....	572
4 ply cellucotton mask.....	259

* An average of 10 experiments was performed with each type of filter.

TABLE 4.—*Bacteria per Ten Cubic Feet of Air**

Control room air.....	185
6 ply gauze mask.....	1,802
6 ply cellucotton mask (no <i>B. prodigiosus</i> recovered).....	210

* In this experiment the subject's mouth was rinsed (gargle) with a 1:100 dilution of a culture of *B. prodigiosus* in saline solution before he talked into the machine. An average of 7 experiments was performed with each type of filter.

came into the opening around the head of the masked subject. This experiment was not what was desired, but it was a great improvement over the old method of using opened Petri dishes of agar to determine the air flora.

Table 3 indicates the average results of 40 experiments. The duration of each experiment varied, but the average was twelve minutes. Plain nutrient agar was the medium used in all instances. Talking into the apparatus was carried out in all experiments except the room air control series. The masked subject would read rapidly in a loud tone. Table 3 gives the results obtained without a mask, with an 8 ply gauze mask from the surgical department and with a 4 ply cellucotton mask. We consider that part of the high bacterial count obtained when the thick gauze mask was used was due to the deflection of the expired air around the mask because of the resistance produced by its thickness. The 4 ply cellucotton mask offers little resistance to the expired air.

Table 4 shows a comparison between a 6 ply gauze mask and a 6 ply cellucotton mask. The cellucotton mask was made by placing 6 plies of this material between two layers of thin, wide-meshed gauze. The

TABLE 5.—*Number of Bacteria Passing Through Filter**

First two minutes.....	20
Second two minutes.....	110
Third two minutes.....	340
Fourth two minutes.....	275
Fifth two minutes.....	317
Total.....	1,062

* The ten minute period of talking was subdivided into five two minute periods. A fresh culture cylinder was inserted at the end of each two minute period. The mouth of the subject was rinsed with a 1:100 dilution of a culture of *B. prodigiosus* before the experiment. A 6 ply gauze mask was borrowed from the operating room for this experiment.

TABLE 6.—*Bacterial Count per Ten Cubic Feet of Air**

Control room air sample.....	170
No mask used.....	887
Hood type mask with 6 ply cellucotton filter (no <i>B. prodigiosus</i> recovered)	178
Hood type mask with 6 ply cellucotton filter; mask too large, poorly fitted; air escaped above (120 <i>B. prodigiosus</i> recovered)	360

* In this series of experiments the subject's mouth was rinsed with a 1:100 dilution of a culture of *B. prodigiosus* in saline solution before he talked into the machine. An average of 4 experiments was performed with each type of filter.

TABLE 7.—*Typical Laboratory Protocol*

Purpose	Cubic Feet of Air per Minute	Time Begun	Time Ended	Incubated	Results
Room control.....	0.75	9:44	9:54	24 hr.	113 colonies
Room control.....	0.83	10:06	10:16	24 hr.	164 colonies
Room control.....	0.90	11:00	11:10	24 hr.	191 colonies
6 ply cellucotton.....	0.785	10:45	10:55	48 hr.	No growth
6 ply cellucotton.....	0.875	10:20	10:30	48 hr.	1 colony (spreader)
6 ply cellucotton.....	0.875	10:57	11:07	48 hr.	No growth
4 ply cellucotton with 2 ply moistened cellucotton between.....	0.875	11:15	11:25	48 hr.	No growth
4 ply cellucotton with 2 ply moistened cellucotton between.....	0.785	2:16	2:26	48 hr.	No growth
4 ply cellucotton with 2 ply moistened cellucotton between.....	0.830	2:31	2:41	48 hr.	No growth
4 ply cellucotton with 2 ply moistened cellucotton between.....	0.875	2:51	3:01	48 hr.	1 colony (spreader)

subject in this experiment rinsed the mouth with a diluted culture of *Bacillus prodigiosus*. This bacterium seldom occurred in control samples of the room air and then only in one or two isolated colonies. We wished to separate the air in the room from the expired air and thought this method would be helpful.

We expected the cotton textiles to be less absorbent for bacteria when they became saturated with water. Table 5 gives the results of

an experiment tending to bear this out. The time was divided into five two minute periods. The same mask was worn for the whole experiment; the cylinder, coated inside with agar, was changed at the end of each two minute period. The subject's mouth was rinsed with a diluted culture of *B. prodigiosus* before the experiment began. It is apparent from table 5 that the permeability of the mask increased during the course of the experiment. It should be borne in mind that the moistened, even saturated, 6 ply gauze mask increases the resistance to passage of the expired air and causes more deflection than does a dry gauze mask.

Table 6 illustrates the influence of proper fitting of the face mask on its efficiency as a filter for expired bacteria. The hood type of mask was used in this experiment. A pocket 6 by 4 inches (15 by 10 cm.) was formed in the mask over the nasal and oral orifices, and 6 ply cellucotton filler was inserted in this pocket. The first mask experiments in table 6 illustrate the results with a head mask properly and tightly fitted to the face of the subject. The next series was performed with a hood mask too large for the subject; it fitted loosely and allowed ready escape of expired air by deflection without filtration.

Table 7 gives the laboratory protocol for one day's experiment. This particular experiment was designed to determine the differences between dry and moist 6 ply cellucotton filters. The material was placed over the funnel connected to the intake of the Wells air centrifuge, and the machine was run for ten minutes. The variations in the bacterial flora of the air are shown in this experiment.

COMMENT

Cellulose wadding of the type used in these experiments can be adapted to filtering bacteria from the air as the air passes through the material. This material is more effective than the cotton gauze generally used in surgical masks. The greatest source of oral bacterial flora in our experiments was escape or deflection of the expelled air during loud talking, above the mask lateral to and on each side of the nose. Our primary problem was one of filtering bacteria from the air. We have done some work with various types and new modifications of face masks. These experiments have not been completed. We are testing various types of mask at this time. A disposable, tightly fitting face mask is now being developed and is already in experimental use. A further report will be made on this subject when we are satisfied that we have something practical, useful and efficient.

Covering of the nose and mouth with an impermeable material deflects the expired air all around the edges of the mask, and the atmospheric pollution is the same as if no mask were worn. We

consider that the problem is one of prevention of atmospheric pollution by filtration, similar to removal of bacterial pollution from water by filtration methods. The droplets in the air, seeded with the bacterial flora of the upper respiratory tract, will find their way downward by gravitation and may be a source of infection. The air currents produced by movements of the persons in the room in opening and closing doors will reduce the effectiveness of the impermeable deflection type of mask to almost zero.

We feel that our experiments show the effectiveness of cellucotton as an air filter. The next problem is to prevent air containing bacterial flora of the upper part of the respiratory tract from leaking around the edges of the mask. We are convinced that if all the expired air can be forced through the cellulose wadding filter the bacteria will remain on the cellulose fibers.

SOLITARY XANTHOMA (LIPOID GRANULOMATOSIS) OF BONE

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AND

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Xanthomatous bone tumor, isolated or multiple, occurring in the absence of the Schüller-Christian syndrome is rare. Recognition of this unusual lesion has proceeded apace with delineation of the Schüller-Christian syndrome.

Bony tumors such as those described by Zeyland and Dega and by Krogus, which seem to be classic examples of giant cell tumor with secondary lipid deposition, bear no resemblance to the type of tumor here described.

REPORT OF A CASE

An Italian boy aged 12 noticed pain and swelling of the left tibial tuberosity five or six weeks before he was first examined, on Oct. 26, 1936. The boy had always been physically active. He remembered no severe injury to his leg or knee, but he had bumped his knee a week previously, while playing football. He had sharp pain on direct pressure over the tibial tuberosity. There was no pain in the left thigh. A diagnosis of Osgood-Schlatter disease (apophysitis) of the left tibial tuberosity was made because of the swelling of the tuberosity and its tenderness to pressure. A roentgenogram, which fortunately included the lower third of the femur, revealed an area of rarefaction at the junction of the lower and the middle third of the femur, suggestive of a bone cyst. It was because of this clinically quiescent lesion of the femur that he was referred by Dr. M. Roth, of Astoria, Long Island.

A bony swelling was palpated on the mesial aspect of the femur, about 2 inches (5 cm.) above the superior border of the patella. This swelling was fixed and slightly tender. It was slightly irregular on its surface and projected a little above the line of the medial femoral cortex. Its base was broad and was a part of the femoral shaft. A cordlike structure ran over its surface. There was no heat of the overlying soft tissues or redness of the skin. General examination gave negative results.

Another roentgenogram of the left femur (fig. 1) showed a roughly ovoid area of rarefaction the size of a silver quarter on the inner side of the bone, at the junction of its middle and lower thirds. The medial cortex was thinned; it bulged slightly at the site of the lesion but was not broken through. Extending proximally from the main lesion, a few smaller, "daughter" areas of rarefaction were seen. The borders of the rarefied areas were lined by sclerotic bone, especially at the lateral part of the main cystic lesion. The lesion was at least one-half the width of the diameter of the shaft of the femur. The larger cyst contained many irregularly placed bony trabeculae which subdivided the lesion into smaller parts. No periosteal reaction or invasion of the soft tissues was noticed.

The lesion seemed benign both clinically and roentgenologically. It was a rarefying lesion of bone with no tendency to bone production. It was peculiar in two respects, its location and its capacity to form daughter lesions. Its location was not typical of bone cyst or of giant cell tumor. It seemed to be an unusual type of benign bone lesion.

On November 2 the tumor was resected (by Dr. Burman). The medial aspect of the femur was approached by a 7 inch longitudinal incision placed antero-medially, the site of tumor being at the center of the incision. The bone was exposed by incision between the vastus medialis and the rectus femoris muscle. The quadriceps bursa was not opened. The periosteum was normal and stripped easily.

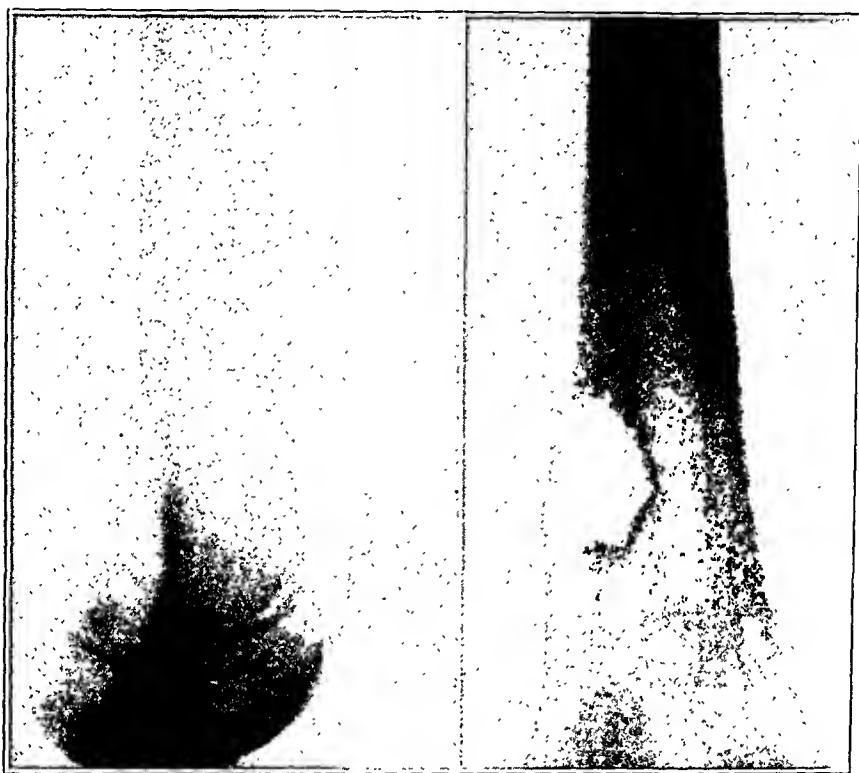


Fig. 1.—Preoperative roentgenogram, taken Oct. 28, 1936, of the xanthomatous femur.

The surface of the bone (which was steel blue) at the level of the tumor was slightly knobby. The tumor was completely resected, the borders of the lesion being carefully measured out with a ruler. The marrow was curetted thoroughly. Total resection of the tumor was verified by a roentgenogram taken immediately, in the operating room (fig. 2).

The gross specimen (fig. 3) consisted of a portion of the shaft of the femur, measuring $2\frac{1}{2}$ inches (6.2 cm.) in length and a little more than one-half the width of the shaft. The medial cortex was thinned and expanded. The medullary cavity was filled with discrete areas of brownish and yellowish tumor tissue. Each yellowish mass was surrounded by a dense capsule of bone, and the intervening regions were also occupied by bone, which was dense and spongy. The largest mass



Fig. 2.—Roentgenogram taken in the operating room after resection of the lesion (Nov. 2, 1936).

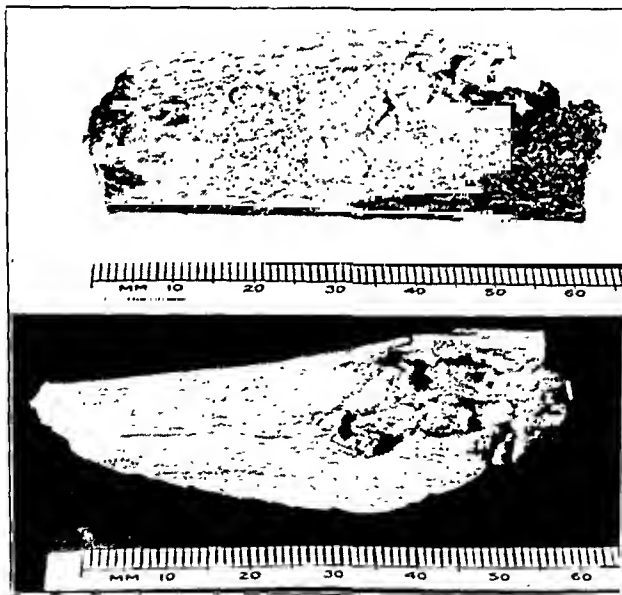


Fig. 3.—Gross specimen. The breaking through of the cortex is a postoperative artefact.

measured $\frac{3}{4}$ by 1 inch (2 by 2.5 cm.) and corresponded to the expanded portion of the cortex. A microscopic diagnosis of lipoid granulomatosis (xanthoma) of bone was made by Dr. Henry Jaffe, pathologist of the Hospital for Joint Diseases. Sections both of bone and of soft tissue showed the presence of lipoid-containing cells aggregated in masses. (These cells probably contained cholesterol ester.)



Fig. 4.—Microscopic picture of a section of resected bone, showing the presence of foam cells.

The larger masses showed giant cells and were associated with a fibrous tissue reaction. Leukocytes were present in such masses. The larger masses were more fibrotic and eroded the cortex.

Roentgenograms of the pelvis, the skull, the ribs and the right femur were taken later, with negative results. The cholesterol content of the blood, with the

patient fasting, was elevated to 224 mg. per hundred cubic centimeters. (The normal value is 150 to 190 mg.) The leg was immobilized in a hip spica for eight weeks and in a long leg cast for four additional weeks. The postoperative course was uneventful, and the wound



Fig. 5.—Roentgenogram taken Jan. 30, 1937, showing no recurrence of the lesion. Note the progressive filling in of the operative defect of the femur.

healed by primary intention. The disease of the left tibial tuberosity healed spontaneously during the period of immobilization. The knee could be flexed only from 180 to 170 degrees when the cast was removed, but after administration of physical therapy flexion became complete.

Inability to flex the knee was due to adherence of the quadriceps muscle to scar tissue at the site of operation. At the time of writing this condition has largely been overcome, and the muscle is soft and flexible.

Periodic check roentgenograms showed no recurrence of the lesion to March 1937 (fig. 4). A roentgenogram taken June 19 (fig. 5) showed recurrence of the tumor. At a point just external to the operative site were three small cyst-like areas. Periostitis was present.

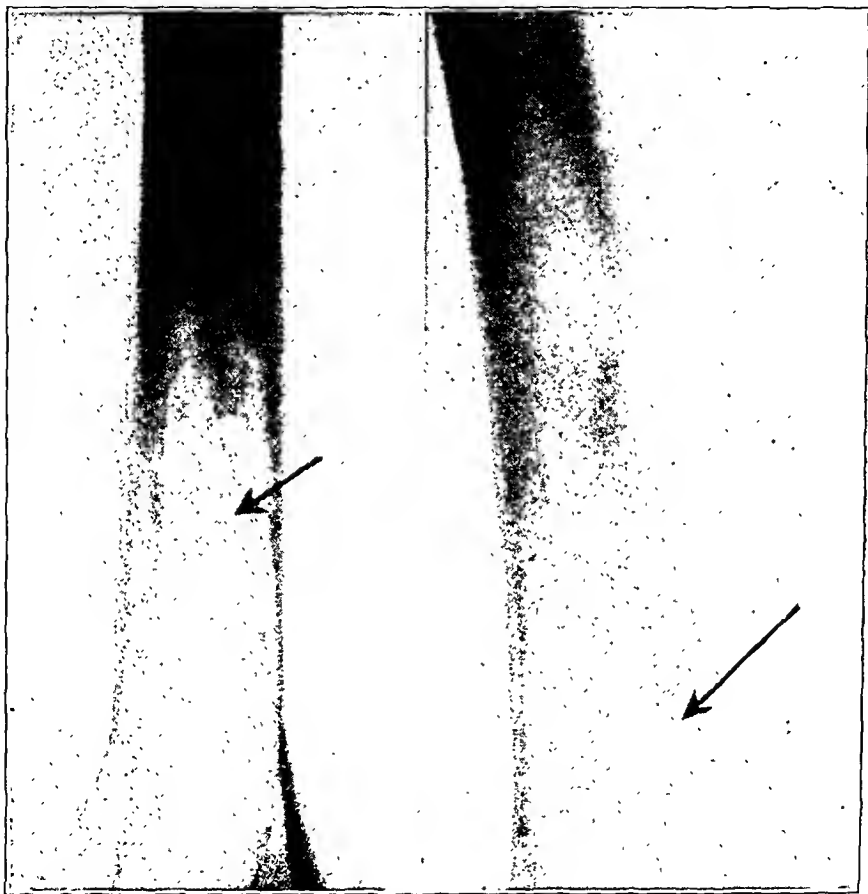


Fig. 6.—Roentgenogram taken June 19, 1937, showing recurrence of the lesion. This is manifested by three round areas of rarefaction, indicated by the arrows. They are better seen in the lateral view. The recurrence is just at the distal part of the resected area.

The patient was given a diet low in cholesterol, and roentgen therapy was begun. The last roentgenogram (fig. 6) showed extensive new bone deposition at the site of the recurrent lesion, which was no longer visible. Two fields, anterior and posterior (10 by 10 cm.), were each given 600 roentgen units at 140 and 150 kilovolts, with filtration of 0.5 mm. of copper plus 1 mm. of aluminum or of 4 mm. of aluminum, at a distance of 40 cm. Six treatments were given, the first three at intervals of one week and the last three at intervals of one month.

The cholesterol content of the blood on June 5 was 200 mg. per hundred cubic centimeters. The patient was last examined on Feb. 11, 1938. His general health was excellent, and he presented no increased urinary output, no prominence of the eyes and no palpable tumors of the skull.

Isolated xanthomatous change of bone is rare. It is likely that multiple osseous involvement, not gross enough to be detected by

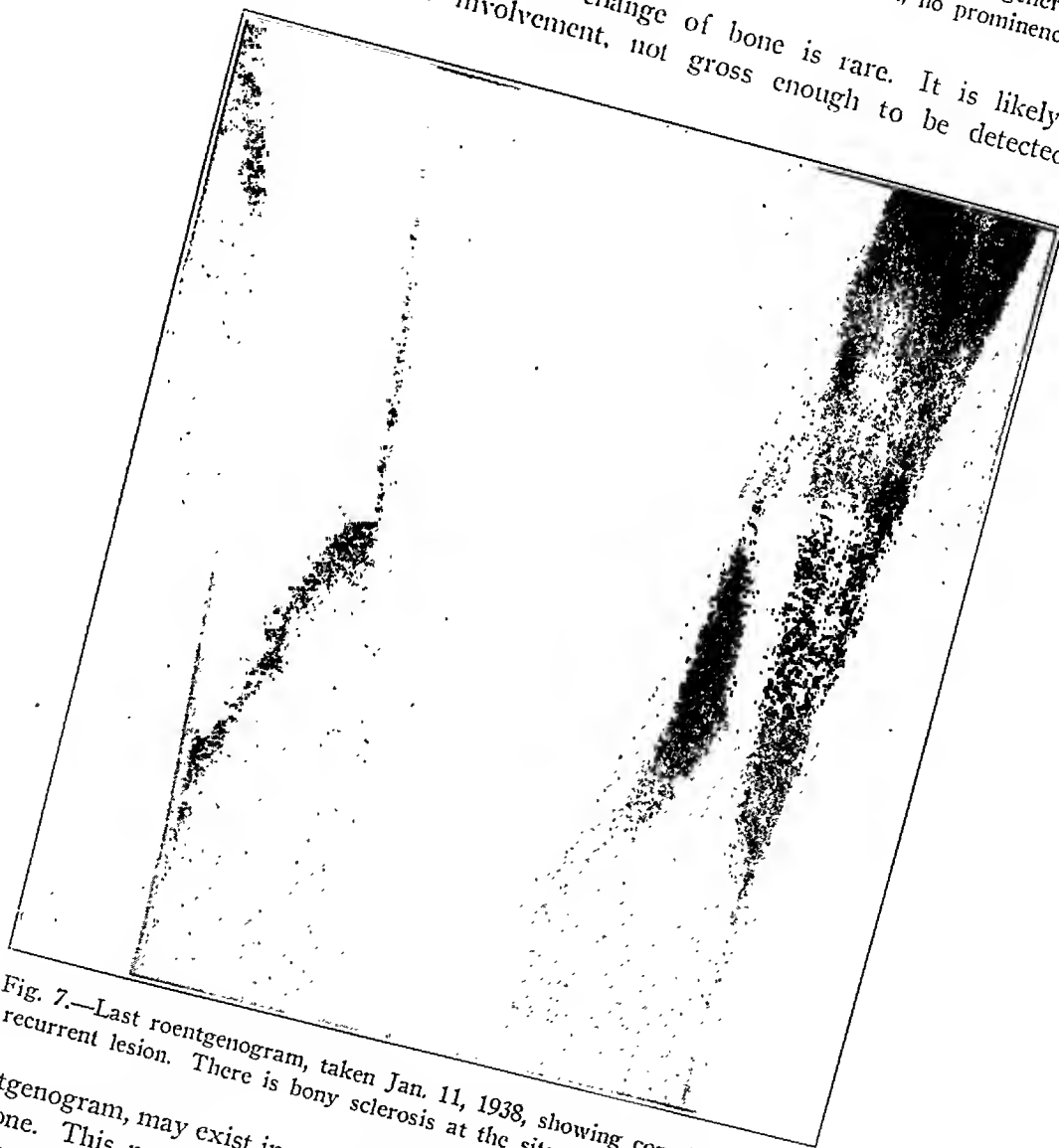


Fig. 7.—Last roentgenogram, taken Jan. 11, 1938, showing complete healing of the recurrent lesion. There is bony sclerosis at the site of resection.

roentgenogram, may exist in such so-called isolated xanthomatous tumors of bone. This may have been true in the case presented. New bony foci may later be recognized, and this can be determined only by a periodic and thorough roentgenographic search of the entire skeleton. Multiple bony foci of bones which are favored by the disease. Multiple bony foci of xanthoma have been described in the absence of the Schüller

Christian syndrome. The latter frequently demonstrates skeletal changes, the most consistent of which (100 per cent) is the change in the skull. Whether there is an ultimate association of the isolated or multiple bony xanthomas here described with the Schüller-Christian syndrome is not answered affirmatively by a study of the reported cases. It is unlikely that such will be the sequence of events in most cases, by reason of age incidence. The age peak of the Schüller-Christian syndrome is usually reached in childhood; isolated or multiple xanthomatosis of bone occurs more often in the third, fourth and fifth decades.

Geschickter and Copeland in a study of 17 cases of Schüller-Christian disease noted that in 2 cases the symptoms of onset were related to solitary lesions in the tibia or the fibula. They described a tumor primary in the fibula, which was seen in 1925. However, a small defect in the skull was noted. In 1934 the patient had multiple skeletal involvement.

ISOLATED FORM

An isolated xanthomatous bone tumor has been described as occurring in a girl aged 12. Our patient was a boy aged 12. The other patients were adults whose ages ranged from 26 to 55.

The disease shows no predilection for either sex. Three patients were males, and 3 were females.

There is no set point from which the disease can be said to begin. Its discovery may be incidental to roentgenographic examination of an adjacent part of the body, investigated for some other cause. This was so in our case, in Phélip's case and in Bahl's case. An approximate length of time, measured by a known injury, would seem to indicate the duration of disease to be from two to twenty-six years, the average being two or three years. A man of 55, with a lesion assumed to be of twenty-six years' duration, noted a mass on the outer side of the upper part of the thigh twenty-six years before. This terminated in an abscess, which maintained itself for fourteen years. Its similarity to a second abscess, of a year's duration, seemed to support this claim.

In 3 cases no trauma was noted. In the remaining cases the trauma was mild, either to the part later affected or to an adjacent part. In no instance was there a single severe sharp or blunt injury to the part. In 1 case there was no remembered history of trauma.

All the patients were in excellent general health.

The patient may have no symptoms. Pain is never severe; it may be absent or it may be intermittent. No redness or heat is noted over the tumor. Swelling is sometimes seen. In 1 case this swelling broke through the skin and discharged necrotic debris containing cholesterol crystals. In another a blood clot developed after an injury above the site of xanthoma. A chestnut-sized tumor ultimately formed at this point,

which was considered sarcomatous on microscopic examination. There may be some question with regard to this diagnosis, since the patient's health remained excellent for three years in the presence of this recurrent tumor, which had not metastasized.

The femur is most often involved in the isolated form of the disease. (The incidence of femoral involvement in Schüller-Christian disease is 26 per cent, according to Lazarewa. This is third in order of frequency, the incidence of femoral involvement ranking below that of invasion of the skull and the pelvis and being equal to that of involvement of the upper jaw.) The epiphysial ends of the bones are spared. In the lower part of the femur the lesion exists at the junction of the middle and the lower third of the bone. This was true of Phélip's patient, a girl of 12, and in our case. Localization, then, was the same for this age group. The upper third of the femur, including the greater trochanter, was involved in 2 patients, each 55 years of age. The lesser trochanter was spared in both. In 1, the disease stopped at the intertrochanteric line, but in the other the neck of the femur was extensively invaded, with ultimate pathologic fracture of the neck, which led to discovery of the xanthoma. The lower third of the fibula and the upper third of the humerus at its junction with the middle third were sites of election in 2 other cases. The proximal phalanx of the right thumb was involved in the final case. This indicates a predilection for the long bones of the body. In only 1 case was there a demonstrable lesion in any of the flat bones. This lesion was an area of rarefaction in the occiput, said not to be characteristic of Schüller-Christian's syndrome. It was not demonstrated clinically. There was no evidence of predilection for the right or the left side of the body.

The tumor is firm and bony hard and is an integral part of its bone. It is sometimes slightly sensitive to pressure. When the tumor becomes superficial, as in the thumb, it distends the overlying skin, which may show dilatation of the fine vessels. The surface of the tumor is finely lobulated or smooth. Ordinarily, it may be difficult of palpation because of its depth of location. Its size is variously estimated, as 2 cm. in diameter, as the size of a plum, as the size of a walnut and as the size of an egg. In only 3 cases did it form a readily visible mass. In the lower third of the fibula it formed a soft, elastic egg-shaped mass; in the thumb, a circular tumor 2 cm. in diameter, and in the upper part of the thigh, a mass which discharged necrotic tissue with cholesterol crystals. The adjacent joint usually shows no disturbance in function. In 1 case there was effusion into the knee joint, which apparently was persistent; its exact relation with the femoral lesion was not adequately determined. One patient noted pain in the left hip for two years on exertion, but the function of the hip was not disturbed till the onset of pathologic fracture of the neck of the femur.

ROENTGENOLOGIC PICTURE

The roentgenologic appearance is that of a benign, delimited, confined bone lesion. Its essential character is osseous rarefaction (replacement by xanthomatous tissue) in the shaft of a long bone. It may be expansile and divided into small cysts by thin bony septums. Small daughter cysts may extend out from the main lesion. Such secondary cysts are irregularly oval and may be longitudinally placed. A fairly thick area of limiting bone sclerosis is noted about each lesion. The cortex adjacent to the lesion may be considerably thinned and even perforated as the result of pathologic fracture. There is no calcification, and no mass in the soft tissues is seen. No tendency to bone production or periosteal involvement is present. The epiphysal ends of long bones are not invaded.

DIFFERENTIAL DIAGNOSIS

In the differential diagnosis the first to be considered is the localized form of osteitis fibrosa cystica. In this disease the entire width of the bone is usually involved, and deformities occur. The lesion is relatively stable and does not tend to increase in size as rapidly as does xanthoma. The cystic divisions of xanthoma are more regular and less diffuse. There is less tendency to pathologic fracture in cases of osteitis fibrosa cystica, and there is increased tendency to distortion. Decalcification of the bone in which the lesion is situated is marked. In the presence of xanthoma, on the other hand, the adjacent bone is normal.

Giant cell tumor is also to be considered. Location of the lesion in the shaft of the bone and tendency to smaller and daughter cyst formation with sclerotic borders are in favor of a diagnosis of xanthoma. Giant cell tumor occurs usually in patients between 20 and 30 years of age and is usually located in the epiphysal end of a long bone. Bone cysts as a rule occur in younger patients (up to about 18) and are usually symmetrically placed in the medullary cavity. They are situated in the proximal ends of long bones, commonly in the humerus, the tibia and the femur. The bone cyst stops at the epiphysal line. Occasionally septums may traverse the cyst, but these are usually few and thin.

Enchondroma in the shaft of a long bone is as uncommon as it is common in the phalanges. It also occupies the entire width of the bone.

The rare adamantinoma is also to be considered. Extradental adamantinoma is found in the tibia.

Echinococcus cysts are very rare. Such a lesion has no limiting sclerotic border. A history of the patient's association at some time with dogs or sheep is usually obtained.

One of us has observed several cases of hemangioma of bone (os calcis). This lesion is also expansile, trabeculated and rarefying. We have never seen it in a long bone. It is characteristically radiosensitive. Osteomyelitis is ruled out by lack of bone production and periostitis, by absence of sequestrums and by the clinical picture (fever, abnormal blood count, local tenderness, redness and pain).

Multiple myeloma occurs in patients past the age of 40. It shows rarefied medullary punched-out areas in many bones, with no bone production and no limiting sclerotic border. The Bence Jones test usually gives positive results. The general condition of the patient serves as a point in differential diagnosis, as it does in cases of metastatic malignant tumor (carcinoma, melanoma).

Metastatic malignant tumor may be single or may involve many bones. The single lesion is usually situated at the site of entrance of the nutrient artery. It is usually erosive and expansile. It is not trabeculated, nor is it encircled by sclerotic borders.

Biopsy is the only sure means of diagnosis, and it is pertinent that in no case was the correct diagnosis made preoperatively. Various diagnoses were made: localized osteitis fibrosa cystica, vacuolar osteitis, melanosarcoma and questionable sarcoma. Some authors made no definite preoperative diagnosis. The procedures used were resection of the tumor in 3 cases when this was possible, curettage of the tumor in 2 cases (the upper end of the femur and the neck of the femur) and guttering of the femur in 1 case, with insertion of fat and a pedicled muscle graft obtained from the quadriceps muscle. The lesion in 1 case was not externally visible when the bone was exposed, and drill holes made through the cortex localized the tumor.

In no case at operation was the periosteum found to be altered. The tumor was usually outlined by sclerotic bone and subdivided into many parts of finer bony septums, between which was a friable, soft tissue, ranging in color from sulfur yellow to chocolate brown. The cortex was sometimes thinned and expanded and in our case was steel blue. In Fürst's case there was invasion of the muscle and skin by the cholesterol-containing tissue, which contained much fatty stuff, resembling, it was said, the material found in cholesteatoma. A necrotic abscess was present. A large number of faceted, pure cholesterol stones were found.

The postoperative course was uneventful in all instances, except in Schrank's case, in which he thought death of the patient imminent. All wounds healed well. The follow-up period is given in only 2 cases. Schrank's patient was observed for eight months. The hip was stiff, and the patient walked well. Consolidation of the rarefied area in the femoral neck was present after curettage. Vermooten's patient was

followed only two months. At the time of writing it is understood that in the remaining cases, although no exact period of follow-up is noted, the patients are in good general health and the diseased area in bone has not increased in size. No note is made of further osseous involvement. No patient has apparently presented any signs of the Schüller-Christian syndrome.

After the nature of the lesion was detected by microscopic examination of the excised tissue, tests to determine the cholesterol content of the blood were done in 3 cases. The cholesterol value in 1 case was 212 mg. per hundred cubic centimeters of blood, a definite elevation above normal. In the remaining 2 cases both free cholesterol and cholesterol esters were estimated. In 1 case the value for free cholesterol was 70 mg., that for cholesterol esters 103 mg. and that for total cholesterol 173 mg. per hundred cubic centimeters. In the final case the value for free cholesterol was 189 mg. per hundred cubic centimeters and that for total cholesterol 231 mg., denoting a definite rise. Bürger's cholesterol feeding test was not done in any case. The value of this test will be commented on later.

Schrank noted that a son of his patient, a boy aged $7\frac{1}{2}$ years, had an area of rarefaction in the right eighth rib. The roentgenologic appearance of this was comparable with the xanthomatous lesion of the left femoral neck of the father. This boy had pleural effusion on the right side, which contained a chylous fluid. He died after an operation for supposed caries of the rib. Postmortem examination was not done.

THE MULTIPLE FORM

The multiple form of skeletal xanthomatosis is as rare as the isolated form. Six cases have been reported. In 4 of these the diagnosis was verified by microscopic examination of tissue, and in 2 (Kienböck and Selda; Kienböck and Schnek) the diagnosis was roentgenographic, based on the previous experience of Kienböck in another case of multiple osseous involvement, in which diagnosis was ultimately made by biopsy. That this experience in repetition is invaluable is proved by the case of Snapper and Parisel, who made the correct diagnosis in their case after publication of the report of Kienböck and Meworach.

The usual working diagnosis has been generalized osteitis fibrosa cystica, and so confident have two of the investigators been of this (Snapper and Parisel; Kienböck and Schnek) that parathyroid exploration was carried out (twice in Snapper and Parisel's case), with completely negative results.

While there are multiple osseous invasions in this form of xanthomatosis, it is usually not as widespread, either generally or locally, as is that of generalized osteitis fibrosa cystica. The smallest number of bones

involved was two and the largest ten, not counting the involvement of phalanges of hands and feet in that case. The usual number of bones involved was two to five. The skull was normal in all instances. The long, tubular bones were again favored, especially the upper part of the femur, its greater trochanter and part of the femoral neck. The humerus was next in frequency, the radius, the ulna, the fibula, the phalanges of the feet and the hands and the metatarsal bones being also affected. Of the flat bones, the left ilium was once involved; invasion of a single rib was seen in 2 cases, and an invasion of three vertebral bodies was noted in only 2 of the 6 cases. The femur was altered in 5 of the 6 cases and the ulna and fibula in 2 cases.

Complete studies are necessary to differentiate multiple xanthomatosis from osteitis fibrosa cystica generalisata (von Recklinghausen's disease). Roentgenologically, as with the localized form of osteitis fibrosa cystica, the bones are malacic and deformed. The areas involved are more extensive. The trabeculae are coarser and thicker and the cystic areas larger and more irregular. More bones are involved in von Recklinghausen's disease, and the disease is more diffuse. There is more tendency to cyst fusion and involvement of the epiphysial ends of long bones. Determination of the calcium content, the phosphorus content and the phosphatase content of the blood is important. Cholesterol studies are helpful in cases of xanthoma.

Multiple myeloma and metastatic malignant tumor must also be considered. These have been previously discussed. In the presence of osteoclastic metastatic malignant tumor, the lesions are purely erosive and perhaps slightly expansile. Bony septums traversing the lesions are not seen. There are no restraining influences. The osteoblastic variety of metastatic malignant tumor need not be considered in differential diagnosis, since it gives rise to osteosclerosis.

There is a rare multiple cystic disease of bone which should be mentioned. It occurs in young persons (up to the age of 20 or 21). It is unilateral. Microscopically the lesion shows fibrous replacement of the bone marrow. Dr. Henry Jaffe has termed it "polyostitic fibrous dysplasia."

The age and sex incidence is similar to that of the isolated form. There were 4 female and 2 male patients. One girl was 10 and 1 boy was 14 at the time of his admission to the hospital. There were 3 patients in the third decade of life, and the oldest was a man of 40.

Trauma plays no great part. A history of competent trauma was not usually given. A boy aged 14 fell 6 feet (1.8 meters) from a hay loft, fracturing the neck of the left femur, through an area of xanthomatous invasion. A slight slip caused pathologic fracture of the surgical neck of the right humerus in another case.

The duration of the disease is again questionable and, as far as it can be determined, it is from two to five years. Study of a patient over a period of years indicates a remarkable stability of the existing lesions, with slight tendency to formation of new lesions. In Kienböck and Meworach's case the development of a visible node on a rib was observed in the course of the disease; in Shelling and Voshell's case the left ilium showed later involvement roentgenographically. Clinically, in this case, several bones later revealed painful thickening of their shafts. Three patients were studied from two to five years.

The disease may be asymptomatic, as in the 2 cases of Chester, in which multiple osseous involvement was observed at autopsy.

Pathologic fracture is more frequent in the multiple form of skeletal xanthomatosis. This depends on the simple mathematical fact of greater probability. The neck of the femur was affected in 2 cases and the surgical neck of the humerus in 1. There may be recurrence of pathologic fracture, and in Snapper and Parisel's case 6 such recurrences were noted. In Kienböck and Schnek's case, two pathologic fractures were noted at the surgical neck of the humerus, and a pathologic subperiosteal greenstick fracture was suspected in point of time between the two evident fractures. The femoral neck united in coxa vara. In Snapper and Parisel's case there were deformity of both femoral shafts and shortening of one lower extremity as compared with the other. In Shelling and Voshell's case there was a coxa vara deformity of the left hip with shortening of the left lower extremity of 3.5 cm. Healing was delayed in Kienböck and Schnek's case, and pseudarthrosis developed after the last pathologic fracture.

Multiple xanthomatous lesions of the skin were present in Merrill's case.

Chemical studies were made in 3 cases. A high value, of 322 mg. of cholesterol per hundred cubic centimeters of blood, was found in Snapper and Parisel's case on one occasion, but on other determinations the content was not above normal. In Shelling and Voshell's case there was an increase of cholesterol in the blood to 221 mg., and in Kienböck and Schnek's case the value was 140 mg. Bürger's test was carried out twice (Snapper and Parisel, Kienböck and Schnek). This test is not reliable or specific of change in cholesterol metabolism. Five grams of cholesterol is dissolved in 50 to 100 Gm. of olive oil and given to the fasting patient. The cholesterol content of the serum should reach a level twice as high four hours later, according to Bürger. Bürger's test gave negative results in both cases, and there was no hypercholesteremia. The value for cholesterol ester is increased over that for free cholesterol in the presence of the Schüller-Christian syndrome, even to five times. Usually 60 to 70 per cent of the total cholesterol is cholesterol

ester. In Snapper and Parisel's case, it was 80 per cent. The calcium content of the blood was 12.6 mg. per hundred cubic centimeters in 1 case and normal (no figures given) in another. In 1 case, in which parathyroid exploration was done at the same operative session when thyroidectomy was done for goiter, the calcium content of the blood was not mentioned. In Shelling and Voshell's case the urinary excretion of calcium was normal, and the value for phosphatase was 8.4 units per hundred cubic centimeters.

We are not including a study of the skeletal changes associated with the Schüller-Christian syndrome or of those atypical forms of this syndrome in which occasional flat or long bones are involved, as in Anspach's case. The Schüller-Christian syndrome may demonstrate all or part of its triad of symptoms—exophthalmos, diabetes insipidus and changes in the skull in association with one or more skeletal xanthomatous lesions. Lazarewa's study is an excellent one for reference.

THERAPY

For the isolated forms of the disease, effective therapy consists of resection of the tumor (when possible) or curettage. When it is possible to establish the diagnosis without biopsy, roentgen therapy, as advocated by Sosman, is the treatment of choice. It is, indeed, definitely indicated for the multiple form of the disease once diagnosis has been made. Ultraviolet irradiation therapy was used by Shelling and Voshell, and the disease was brought to a standstill. A diet low in cholesterol should be tried, especially in cases of multiple skeletal xanthomatosis with hypercholesteremia.

The ultimate fate of the patient is not indicated in any of these case reports. There were no fatalities, but no patient can be said to be definitely cured. The disease is relatively stationary, but new bone foci may develop, since the illness is a generalized metabolic disease. The isolated lesion is, then, only fortuitous or apparent. Function is disturbed in the not infrequent presence of pathologic fracture, and healing may be delayed or deformity may develop.

BIBLIOGRAPHY

- Anspach, W. E.: Xanthomatosis with Involvement of a Vertebral Body, *Am. J. Dis. Child.* **48**:346 (Aug.) 1934.
 Bahls, G.: Ueber ein solitäres Xanthom im Knochen, *Zentralbl. f. Chir.* **63**:1041, 1933.
 Chester, W.: Ueber Lipoidgranulomatose, *Virchows Arch. f. path. Anat.* **279**: 561, 1930.
 Fürst, A.: Central Xanthomatous Tumor of the Femur, *Časop. lēk. česk.* (nos. 18-19) **75**:522, 1936.
 Geschickter, C. F., and Copeland, M. M.: Tumors of Bone (Including the Jaws and Joints), revised edition, New York, American Journal of Cancer, 1936, pp. 657 and 658.

- Kienböck, R., and Meworach, L.: Ein Fall von multiplen Xanthomen in den Knochen, *Röntgenpraxis* **4**:76, 1932.
- and Schnek, F.: Ein Fall von Xanthomatose des Skeletts, *Beitr. z. klin. Chir.* **156**:237, 1932.
- and Selda, A.: Ueber die multiplen Xanthome der Knochen, *Fortschr. a. d. Geb. d. Röntgenstrahlen* **48**:328, 1933.
- Krogus, A.: Zur Frage der Knochenzysten und Riesenzellentumoren, *Acta chir. Scandinav.* **59**:1, 1925-1926.
- Lazarewa, A.: Die Knochenform der Xanthomatose, *Fortschr. a. d. Geb. d. Röntgenstrahlen* **45**:692, 1932.
- Merrill, A. S.: Case of Xanthoma Showing Multiple Bone Lesions, *Am. J. Roentgenol.* **7**:480, 1926.
- Phélip, J. A.: Ostéite kystique vacuolaire juvenile xanthomateuse de l'extrémité inférieure du fémur, *Bull. et mem. Soc. nat. de chir.* **61**:443, 1935.
- Schrank, H.: Eine Lipoidgranulomatose im Oberschenkelhals, *Zentralbl. f. Chir.* **60**:1641, 1933.
- Schröder, F.: Ein zentraler xanthomatöser Riesenzellentumor der Fibula, gleichzeitig ein Beitrag zur Kenntnis der xanthomatösen Gewebsneubildungen, *Arch. f. klin. Chir.* **168**:118, 1931.
- Shelling, D. H., and Voshell, A. F.: Xanthomatosis Generalisata Ossium: Report of a Case Simulating Osteitis Fibrosa Cystica, *Arch. Int. Med.* **55**:592 (April) 1935.
- Sinberg, S. E.: Echinococcus Cyst of the Sternum, *Radiology* **27**:736, 1936.
- Snapper, I., and Parisel, C.: Xanthomatosis Generalisata Ossium, *Quart. J. Med.* **2**:407, 1933.
- Sosman, cited by Golden, R.: *Diagnostic Roentgenology*, New York, Thomas Nelson & Sons, 1936, p. 479.
- Vermooten, V.: Xanthosarcoma of Thumb: A Central Benign Giant Cell Tumor of the Proximal Phalanx of the Thumb, *Ann. Surg.* **81**:851, 1925.
- Zeyland, J., and Dega, W.: Ostitis Fibrosa mit Lipoidzellen, *Arch. f. klin. Chir.* **150**:310, 1928.

SIXTY-SEVENTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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NEW YORK

HEREDITARY AND DEVELOPMENTAL DEFORMITIES

Chondrodystrophy with Flattening of the Vertebrae.—Guerin and Lachapele¹ report a case of chondrodystrophy, the patient being a boy aged 7. They label the condition in this case "platybrachyspondylie," since the vertebrae, particularly in the lower portion of the dorsal region, were large and flat, each tending to end anteriorly in a pointed extremity. This resulted in moderate dorsal kyphosis. Associated abnormalities of the skeleton in other regions were also found. In both feet there was a tendency to hallux valgus. The first metatarsal bone was large and short, with a large epiphysis. The second, third and fourth metatarsal bones were curved medially. In place of the scaphoid and the first cuneiform bone there were several ill defined centers of ossification and the second and the third cuneiform bone were fused. Both hips exhibited coxa vara deformity. There was general retardation in the development of most of the skeletal epiphyses. In reviewing the literature the authors found reports of 22 similar cases, with slight variations in the associated skeletal abnormalities. The authors feel that in cases of chondrodystrophy of the spine other skeletal defects would be found more often if roentgenograms of the remainder of the skeleton were taken routinely.

This report of progress is based on a review of 141 articles selected from 225 titles relating to orthopedic surgery and appearing in the medical literature approximately between March 1 and July 1, 1938.

1. Guerin, R., and Lachapele, A. P.: *Rev. d'orthop.* 25:23, 1938.

Chondrodystrophy.—Sargent ² had the opportunity to study 10 adults suffering from chondrodystrophia foetalis, 3 females and 7 males. The author believes that only the milder forms of this disease permit the patient to reach adult life. The disease appears to be transmitted by males. Roentgenologic and serologic studies showed no other disease in these patients.

Atypical Chondrodystrophy.—Marquardt ³ describes 7 cases of growth disturbance. The first 3 are typical cases of chondrodysplasia. The second group consists of the cases of 2 sisters. One of these cases is typical. The case of the other sister is only suggestive of the lesion, presenting multiple mild epiphyseal disturbances. The third group consists of 2 cases in which there were multiple abnormalities of cartilaginous growth. The author, on the basis of roentgen findings in the pelvis, the vertebrae and the knees similar to those seen in cases of chondrodysplasia, suggests that these are atypical cases and that many fleeting transitional types of such disturbance probably exist.

Infantile Kyphosis.—Frejka ⁴ points out that dorsal kyphosis is not uncommon in children between the ages of 4 and 14 and that there is a definite relation between kyphosis and nasal obstruction. About 80 per cent of a group of children with nasal obstruction due to adenoids showed some degree of increased dorsal kyphosis. Nasal obstruction by adenoid tissue or by chronic mucosal hypertrophy necessitates mouth breathing, and this superficial breathing is accomplished by means of the diaphragm, the abdominal muscles and the lower part of the thorax. The upper part of the thorax is not used and remains in the position of expiration. This results in the thoracic vertebral column remaining in the position of expiration, curved forward to form an arc at the back. As the child grows the curve becomes more pronounced and more rigid. Treatment consists first in removal of the nasal obstruction and subsequently in training directed toward breathing through the nose and with the thoracic cage. Good results are obtained if treatment is undertaken before the curve becomes rigid.

[ED. NOTE.—A similar deformity has been observed in children suffering from asthma.]

TUBERCULOSIS

Treatment of Tuberculosis of the Foot.—Calve ⁵ states that tuberculous infection accentuates the anatomic differences between the foot of an adult and that of a child. In a small child the great amount of cartilage surrounding the bony muscles of the tarsal bone preserves the

2. Sargent, W. S.: U. S. Nav. M. Bull. **36**:67, 1938.

3. Marquardt, W.: Arch. f. orthop. u. Unfall-Chir. **38**:711, 1938.

4. Frejka, B.: Rev. d'orthop. **25**:110, 1938.

5. Calve, J.: Bull. Soc. belge d'orthop. **10**:175, 1938.

form of the bone and protects the articulations from infection. In a child with tuberculosis of the foot, healing may occur or a fistula may develop. A minimum of two years is required for healing. During this period there should be complete immobilization and no attempt at standing. If healing is long delayed in a case of tibiotarsal infection, one may perform an astragalectomy. If secondary infection has occurred, adequate drainage is the first requirement. Astragalectomy is advised for drainage in the posterior part of the foot. For the distal tarsal bones bilateral drainage is advocated, with resection of the bone if necessary. Healing is often surprisingly good. The shape of the foot should be preserved if possible. Amputation should never be performed on children. Constant watch must be kept to prevent severe deformity. In adults, healing occurs in a fair number of cases after prolonged immobilization. When healing does not occur and secondary infection intervenes, amputation of the foot offers the best chance of cure. Resection and astragalectomy should not be performed on adults.

POLIOMYELITIS

Treatment of Acute Poliomyelitis.—Mills⁶ gives an account of the so-called "Sister Kenny Treatment." This method of treatment has been used in a "chain" of 1,400 cases in Australia but in only 35 cases in which the condition was in an early stage. In contradistinction to the orthodox methods, comprising rest, immobilization in neutral position, splinting and subsequent massage, the view is taken that the muscular pain results from venous engorgement and consequent anoxemia of the paralyzed vessels and that the limbs must be treated eventually by fomentations and hydrotherapy to restore capillary tone and by movement through the full range of each joint every two hours. Pain and tenderness always respond to such treatment within three days, and a graded system of reeducation is started, usually within the first week of paralytic manifestations. It is claimed that in no patient treated by this method has deformity developed and that there has been no tropic disturbance, such as chilblains or impairment of growth.

[ED. NOTE.—This technic is now being tried at Queen Mary's Hospital, Carshalton, England, where a ward has been set aside for the purpose. It is doubtful whether it will be long continued when the end results are compared with those following the commonly accepted treatment as reviewed in the last report of progress.]

CHRONIC ARTHRITIS

Gonorrheal Arthritis.—Criteria for diagnosis of gonococcic arthritis are, according to Spink and Keefer:⁷ (1) local gonococcic infection

6. Mills, F. H.: Brit. M. J. **1**:168, 1938.

7. Spink, W. W., and Keefer, C. S.: New England J. Med. **218**:453, 1938.

immediately preceding the attack of arthritis or occurring at the same time, (2) smears and cultures of urethral or cervical exudates revealing gonococci, (3) positive reactions to gonococcic complement fixation tests of either the blood serum or the synovial fluid, and (4) gonococci in the aspirated contents of the joints or tendon sheaths. Treatment was instituted in three groups of patients as follows: Group 1 consisted of 26 patients treated by medical means only. Group 2 consisted of 24 patients with effusion into one or more joints, treated with aspiration. Group 3 included 20 patients with purulent articular effusion treated with surgical drainage. Follow-up studies revealed that 20 of the 26 patients in group 1 were free of all articular symptoms and had no limitation of motion; 14 of the 24 patients in group 2 showed no limitation; 3 of the 20 patients in group 3 had complete articular function. Hyperthermia was not used in these cases, and sulfanilamide was not given.

Multiple Hydrarthroses in Chronic Rheumatism.—Ravault and Leger⁸ report 2 cases of what they believe to be a distinct form of arthritis, to which they give the name "synovial dropsy." The condition in their cases was characterized by an insidious onset of effusion into the large joints, particularly those of the knees. The effusions were large. In 1 case there was also a collection of fluid in one of the flexor tendon sheaths. The patients suffered little pain. There was no tendency to ankylosis, the only limitation of motion being from the tension of the articular fluid. In 1 case no destruction of the joint surfaces was noted by roentgenograms even after thirteen years. The effusions were characterized by their extreme chronicity and their tendency to recurrence in spite of many different kinds of therapy. In searching for a cause of this peculiar articular disease the authors eliminated gonorrhea, syphilis, tuberculosis and gout. They were unable to assign to it any definite cause.

THE BACK

Lesions of the Intervertebral Disks and Ligamentum Flavum.—Naffziger⁹ gives a clear and detailed description of the normal and pathologic anatomy of the intervertebral disks and the ligamentum flavum. The anatomic findings are correlated with symptoms and treatment. The anatomic side of the subject is illustrated with enough clinical data to lend practical interest.

[Ed. NOTE.—This is an excellent paper, well illustrated and well worth reading as a foundation for study of any of the recent clinical and statistical studies on these conditions.]

8. Ravault, P. P., and Leger, G.: *Lyon méd.* 161:81, 1938.

9. Naffziger, H. C.; Inman, V., and Saunders, J. B. M.: *Surg., Gynec. & Obst.* 66:288, 1938.

Active Braces for Scoliosis.—Wolf¹⁰ reviews the historical development of braces for the correction of scoliosis. The deformities for which correction is sought are: (1) curvature of the spine, (2) overhang of the spine in relation to the pelvis, (3) torsion and hump formation, and (4) diminution in height of the body. Most braces attempt three point pressure, i. e., pressure at both ends and at the apex of the curvature. The force cannot be made to act on the spine itself but must be applied through the ribs. For force to be exerted on the apex of the curve the force must be directed below the apex, since the ribs follow a downward direction. Pressure must also be applied obliquely. Axillary crutches can exert pressure only on the ribs; they cannot lift the shoulder girdle. Lateral displacement of the thorax can be improved by pushing on the same side with a pad against the pelvis or by pulling with a thigh band on the contralateral side. Scoliosis cannot be corrected by braces alone but correction can be continued by such means after the spine has been somewhat mobilized.

OSTEOMYELITIS AND SUPPURATIVE INFECTIONS.

Osteomyelitis Caused by Friedländer's Bacillus.—Septicemia and osteomyelitis caused by Friedländer's bacillus occur most commonly in adults. Talbot and Parlange¹¹ report 1 case and review 5 others from the medical literature. This type of osteomyelitis is apparently rare and is always serious, death frequently resulting from septicemia; in 3 of the 6 reported cases the patients died. The diagnosis is made from bacteriologic examination. Neither the clinical nor the roentgenologic appearance differs from the usual pathologic picture of osteomyelitis. Treatment is chiefly general and is directed toward relief of symptoms. Drainage is performed only when there is definite abscess formation.

Pyemic Articular Metastases.—Wiesman¹² reports 4 postmortem examinations in which pyemic articular metastases were observed. In 3 cases the sacroiliac joints (among others) were involved, and in 1, suppurative arthritis of the occipitoatlantoid joint and of the atlanto-epistrophic joint was observed. In the last-mentioned case cervical symptoms developed three days after a tonsillectomy. Wiesman analyzes the distribution of articular lesions in the protocols of 52 cases of pyemia observed in the pathological institute of the University of Zurich, Switzerland. The knee was by far the most often affected. The other major joints of the extremities were involved less frequently. Symmetric involvement was observed in one fifth of the cases. The infection was mainly streptococcic.

10. Wolf, J.: Am. J. Surg. **39**:557, 1938.

11. Talbot and Parlange: Rev. de chir., Paris **76**:271, 1938.

12. Wiesman, E.: Deutsche Ztschr. f. Chir. **249**:221, 1938.

Roentgen Diagnosis of Osteomyelitis of the Vertebrae.—McNutt¹³ reports in detail 2 cases of osteomyelitis of the vertebrae and includes an excellent review of the literature. In the acute form the disease is associated with high temperature, severe pain, prostration and high mortality. Paralysis is a frequent complication. The chronic form is milder in all its aspects and probably occurs as frequently as the acute form. The disease occurs more frequently in males than in females. Any portion of the vertebral column may be affected, but the most frequent site is the lumbar region, the next in order being the cervical, the dorsal and the sacral region. Early in the disease the roentgenogram may be normal or may show only slight haziness; later the changes may be characteristic of rarefying and proliferating osteitis. Commonly the condition develops as a destructive bone lesion which early shows new bone formation.

Surgical Principles in Treatment of Infections of the Hand.—Koch¹⁴ outlines simple procedures whereby infection may often be prevented after an injury to the hand. If the patient is seen immediately the wound is thoroughly washed with soap and sterile water applied with soft cotton. When this is done infection rarely follows. The wounds are sutured immediately. Infection occurs more often when wounds are not treated for several days. When infection has taken place the first essential is absolute rest. An attempt is made to localize the infection with large, warm, wet sterile dressings. Roentgen treatment of $\frac{1}{2}$ erythema dose, repeated in forty-eight hours, seems to be helpful. Ice packs are contraindicated for an infection of this type. Conservative treatment should be continued until localization of the infection has occurred. For each condition there is one best method of drainage. Operation should be performed with the region under a tourniquet. Rest and warm wet dressings should be continued after drainage has been instituted. If infection is unduly persistent a foreign body, sometimes a necrotic tendon or a bony sequestrum, should be suspected. The removal of the foreign body should be carried out gently. After infection subsides, function should be restored if possible.

Immobilization and Posture in Treatment of Infections of the Extremities.—Wangensteen,¹⁵ writing on acute infections of the extremities, states that "an inch of gravity operating for three days will accomplish as much as three weeks of heat and massage." Accordingly, he advocates rigid immobilization and elevation of the affected member in cases of infection. He prefers using immobilization by a plaster cast with appropriate windows for dressings to other methods of immobilization. He believes that one should strive for physical immobility and elevation, keeping the swelling at a minimum.

13. McNutt, J. R.: *Am. J. Roentgenol.* **39**:52, 1938.

14. Koch, S. L.: *West. J. Surg.* **46**:301, 1938.

15. Wangensteen, C. H.: *Minnesota Med.* **21**:225, 1938.

NEOPLASMS

Primary Adamantinoma of the Tibia.—This tumor, which originates from dental enamel, is of extremely rare occurrence elsewhere than in the jaw. Dunne¹⁶ found only 6 cases in the literature, which he analyzes and discusses. A typical case is reported in detail, with photographs, roentgenograms and photomicrographs. Although diagnosis of this tumor is difficult to make by means of roentgenograms, biopsy of material obtained by aspiration is a safe and valuable procedure. Treatment consists of (1) amputation (if the tumor is extensive as in the case reported), or (2) resection (if the involvement is not great and if no cell pockets are overlooked). Irradiation has proved disappointing except for some tumors of the jaw. The author feels that amputation should provide complete and lasting cure.

Benign Osseous Lesions Showing Invasion of Bone by Spindle Cells.—Murphy¹⁷ reports 4 cases of benign osseous lesions with invasion of bone by spindle cells, in which the lesions were treated with excellent results by means of the roentgen rays. In 3 cases the condition was caused by a low grade infection. In the fourth case the lesion was a giant cell variety of osteitis fibrosa cystica.

Hematologic Diagnosis of Multiple Myeloma.—Zadek¹⁸ has been able to make a diagnosis of multiple myeloma by vital staining of marrow obtained by sternal puncture. He believes that the disease can at times be diagnosed by the finding of lymphoid or plasma cellular reticulum cells with "nuclear granules."

Primary Bone Tumor in Children.—Coley and Peterson¹⁹ discuss the primary tumors of bone observed in children. Primary bone tumors are more frequently malignant in children than in adults. Diagnosis is often difficult. Pain in children is often to be explained on a rheumatic basis. Pain for which no definite cause can be found indicates roentgen examination of the extremity. One should not wait for the development of swelling. A study of the phosphatase, calcium and phosphorus content of the blood is sometimes of value. Biopsy of material obtained by aspiration is sometimes helpful. The common benign tumors are solitary bone cyst, giant cell tumor, chondroma, osteoma and multiple congenital chondrodysplasia. The common malignant tumors are osteogenic sarcoma, endothelioma and liposarcoma. These are best treated by roentgen therapy. Other malignant tumors are usually treated surgically if they are accessible.

16. Dunne, R. E.: New England J. Med. **218**:634, 1938.

17. Murphy, J. T.: Am. J. Roentgenol. **39**:586, 1938.

18. Zadek, I.: Wien. klin. Wchnschr. **23**:632, 1938.

19. Coley, B. L., and Peterson, R. L.: Am. J. Surg. **39**:334, 1938.

MUSCULAR INJURIES

Rupture of the Biceps Brachii Muscle.—Waugh²⁰ believes that rupture of the biceps brachii muscle is not uncommon but is often unrecognized. He reports the cases of 14 patients admitted to the United States Marine Hospital in San Francisco and to the New Orleans Hospital and Dispensary for Women and Children. The injury was due to indirect trauma in 7 cases and to direct trauma in 4. In 1 it followed a stabbing injury, and in 2 the cause was uncertain. Among those in which it was caused by indirect trauma, a positive Wassermann reaction was obtained in 3. Rupture of the muscle may occur at any site. The long head of the biceps muscle is most frequently ruptured (12 of the reported cases). Rupture in the bicipital groove is usually the result of degenerative changes. Rupture below the bicipital groove is common in direct trauma. The short head of the biceps muscle was torn in 2 cases. The symptoms and signs were variable. There was always a history of trauma followed by pain, weakness in the arm and discomfort in the shoulder. In the cases reported the most constant sign was a deformity in the contour of the biceps muscle. Twelve of the 14 patients were operated on. Rupture of the long tendon was usually easily repaired. A tear at the myotendinous junction usually required a fascial transplant. For partial rupture the author advises rest with the tendon in a position of relaxation.

Tenosynovitis of the Long Head of the Biceps Brachii Muscle.—Tenosynovitis of the long head of the biceps muscle was found by Schrager²¹ to be the most common cause of extra-articular pain in the shoulder joint in his cases. Trauma was the chief cause. Pain was definitely localized in the bicipital groove, and motion was limited much as in cases of bursitis. Schrager's treatment consists of heat and rest followed by diathermy and in cases of severe involvement by faradism. In some cases improvement is obtained by sudden traction on the arm while it is relaxed and abducted.

MISCELLANEOUS

Articular Osteochondroma.—Curnevali²² studied microscopically osteochondromatous nodules removed from the knees of patients. These nodules were in the final stage of a proliferating process. The cartilage had been preserved by osmotic nutrition, with resulting hyperplasia of the synovial membrane. This was followed by secondary metaplasia of the enlarged synovial villi into chondromatous nodules. Curnevali states that ossification progresses as long as the nodules have vascular connections.

20. Waugh, R. L.: South. M. J. **31**:619, 1938.

21. Schrager, V. L.: Surg., Gynec. & Obst. **66**:785, 1938.

22. Curnevali, S. L.: Arch. di ortop. **53**:713, 1938.

Spontaneous Osseous Fissures.—Leriche and Jung²³ describe the case of a woman aged 38 who complained of dull pain in the region of both hips for three years. There was no history of trauma or illness. Roentgen examination revealed three cortical cracks, one in the inferior portion of the medial cortex of each femoral neck and one in the descending ramus of the pubis. There was slight periosteal reaction around each. The calcium content of both the serum and the urine was low, bordering on the values found in cases of tetany. Parathyroid extract, lime salts, vitamin D and ultraviolet irradiation were given. Eight weeks later the pains had greatly diminished. The values for calcium were approximately the same as when the patient was first seen. The authors mention 4 similar cases which they found reported in the literature. They offer no solution but feel that there is some underlying fault in the growth of the bones which produces this picture.

[ED. NOTE.—The condition in these cases is similar to the “pseudo-fracture” of the tibia recently reported but not as yet published by one of the editors.]

Spurs on the Os Calcis.—Steindler and Smith²⁴ contrasted two series of patients with painful spurs of the os calcis, one group being given conservative treatment with foot supports and the other being given operative treatment. There was very little to choose between the results in the two groups. Symptoms were controlled in 46.4 per cent of the patients conservatively treated. The percentage of successful operations was 59. The authors concluded that the symptoms of painful heel with spur of the os calcis may be controlled in about half the cases by conservative measures. When conservative treatment fails, operation is indicated. In the authors' cases, if simple excision of the spur was followed by recurrence a rotation osteotomy of the os calcis was performed.

Posterior Hernia of the Knee Joint.—Haggart²⁵ states that although a posterior hernia of the knee joint may simulate an internal derangement of the knee, the condition is correctly diagnosed when cystic swelling is found in the popliteal space, located usually in the midline and distal to the cutaneous flexion crease in this region. Clinically the symptoms vary from aching discomfort to severe, binding pain in the region of the knee, often associated with intermittent effusions into the knee joint and with moderate to marked disability. The hernial sac usually communicates with the joint by a pedicle 1 or 2 cm. in length, arising either above or below the oblique popliteal ligament. The hernial sac may occasionally dissect its way down the leg to the region of the

23. Leriche, R., and Jung, A.: *Lyon chir.* **35**:47, 1938.

24. Steindler, A., and Smith, A. R.: *Surg., Gynec. & Obst.* **66**:663, 1938.

25. Haggart, G. E.: *J. Bone & Joint Surg.* **20**:363, 1938.

midshaft and lie on top of the gastrocnemius muscle and beneath the deep fascia. Excellent drawings illustrating the anatomy of the region of the knee joint accompany Haggart's article. Microscopic examination reveals the lining of the hernial sac to be true mesothelium which cannot be distinguished from the synovial membrane of the knee joint. Signs of acute and chronic inflammation are present. Treatment is operative removal of the sac. An incision is made in the midline over the site of the swelling, the lower end of the incision being carried to the medial or the lateral side, depending upon the location of the sac. After division of the deep fascia, inspection reveals a fibroserous wall of the sac, which is freed by sharp dissection, beginning at the distal portion. It is necessary to divide some of the tendon and fibers of the gastrocnemius muscle. The popliteal nerves and vessels are displaced to the lateral side of the leg. When the sac is entirely free the pedicle is clamped, tied and cut. The stump is then inverted into the knee joint, and the foramen in the capsule is closed with heavy silk mattress sutures. A posterior plaster splint with the knee in full extension is applied for ten days. Exercises for "setting" the quadriceps muscle are given during this stage. Early weight bearing (with the patient on crutches) is encouraged.

ORTHOPEDIC OPERATIONS

Use of Os Purum in Bone Implantation.—Os purum, i. e., bone treated physicochemically, freed of connective tissue, fat and protein and then cleansed, was used by Orell²⁶ to promote bony healing in cases of tuberculosis of bones and joints. In both compact and spongy form the material was used to fill osseous defects left by surgical procedures and to fix (fuse) adjacent parts of the skeleton after resection of diseased tissue. By this method the author was successful in securing ankylosis of resected ankle joints in 6 of 8 cases. In 14 cases of arthrodesis of the knee the treatment was successful. Five shoulders were successfully fused. In addition some cases are reported in which tuberculous foci in the metacarpal or the metatarsal bones, the os calcis, the tibia, the femur and the pelvis were curetted and packed with os purum, with apparent healing. Most of the cases reported were followed for several years. The advantages of os purum are: (1) It may be stored for long periods; (2) there is no limit to the size and shape of the material used, and (3) an accessory operation to obtain fresh autoplasmic bone is not necessary.

New Operative Treatment for Congenital Dislocation of the Hip.—Krinitzky²⁷ describes a new operation for congenital dislocation of the hip, to be used in "old" cases in which the dislocation cannot be reduced

26. Orell, S.: Surg., Gynec. & Obst. 66:23, 1938.

27. Krinitzky, J. M.: Lyon chir. 35:188, 1938.

bloodlessly. It consists in introducing a bone peg transversely through the subtrochanteric region of the femur until it enters the old acetabulum. The operation is done through a lateral incision over the upper femoral shaft, the direction and point of entry of the peg having been previously calculated by means of fluoroscopic examination. The desired objective is that the end of the peg shall lodge beneath the roof of the old acetabulum, so that when weight is borne on the leg the femur is prevented from riding up and rotation is limited. Six cases are reported, with follow-up during postoperative periods of six to twenty-two months. In all cases the limp was much lessened and stability was obtained. In 2 cases the bone peg increased in size.

Resection of the Elbow Joint.—Davidson and Horwitz²⁸ report 17 cases of resection of the elbow joint. In 2, resection was done for tuberculosis; in 13, for comminuted fractures or fracture-dislocations, and in 2, for old, irreducible dislocations of the elbow joint. Davidson and Horwitz used a longitudinal posterior incision, retracing the triceps tendon with a portion of the olecranon to expose the joint. About 1 inch (2.5 cm.) of the humerus and $\frac{1}{2}$ to 1 inch (1.2 to 2.5 cm.) of the ulna and radius are resected. The results have been satisfactory for 9 adult patients but for only 2 children. Of the remaining children in the series (5), 2 showed fair results and 3 had ankylosis. One case is too recent for evaluation of the result. The authors concluded that the operation is satisfactory for adults and is at present the treatment of choice for tuberculous arthritis when conservative therapy has failed. It is contraindicated for children prior to the cessation of growth.

[ED. NOTE.—Fusion of the elbow joint in a useful position for function is the usually accepted therapy for tuberculosis when conservative treatment fails. For traumatic conditions with destruction of the elbow an arthroplasty with interposition of fascia seems to give a better and more stable joint.]

Major Amputations in the Aged.—Findley²⁹ reports 72 cases of major amputation of the lower extremity, in which 57 of the patients were treated at the New York City Hospital and at the Beekman Street Hospital, a private institution. Most of the patients in the first group were old and were surgically "poor risks," having arteriosclerotic or diabetic gangrene. The general mortality in this group was 54.4 per cent, while in the latter group the mortality was 46 per cent. Findley advises early operation and midthigh amputation. He uses the guillotine flap method without a tourniquet, with through and through sutures and drainage. Anesthesia induced with nitrogen monoxide and oxygen anesthesia is used. He advocates a speedy operation, that is, one per-

28. Davidson, A. J., and Horwitz, M. T.: *Surgery* 3:226, 1938.
29. Findley, R. T.: *Am. J. Surg.* 39:46, 1938.

formed within twenty minutes. In the first group, arteriosclerosis was the cause of disease in 32 per cent of the cases, diabetic gangrene in 32 per cent, thromboangiitis obliterans in 14 per cent and osteomyelitis in 9 per cent. In the second group, trauma alone was a factor in 47 per cent of the cases, embolism in 20 per cent, osteomyelitis in 13 per cent, diabetes in 7 per cent and diabetes with arteriosclerosis in 7 per cent. The average age in the second group was 43 and that in the first group 57 years.

Transplantation of the Brachioradialis Muscle for Weakness of the Triceps Muscle.—Ober and Barr³⁰ report a method of using the brachioradialis muscle for paralysis of the triceps muscle in cases of poliomyelitis. The brachioradialis muscle is exposed by an incision 4 inches (10 cm.) above the lateral epicondyle, extending downward on the posterolateral aspect of the humerus to 4 inches below the radial head on the lateral side of the forearm. The anterior margin of the brachioradialis muscle is defined, and its nerve and blood supply are found. The free anterior margin of the brachioradialis is rolled laterally and is sutured to the fascia and periosteum along the subcutaneous edge of the ulna, to the olecranon and to the triceps tendon. The arm is immobilized in full extension and supination. Exercises are started in ten days. Five patients have been operated on, and in all of them great improvement of function in extending the elbow has been noted.

Operation to Improve Function in Cases of Paralysis of the Quadriceps Muscle.—Yount³¹ modifies his original operative technic³² by a more radical dissection of the fascia lata in order to utilize effectively the muscular power available in the gluteus maximus muscle. Also, the biceps muscle is mobilized more freely in order to improve its direction of pull. By means of a long cutaneous incision the long head of the biceps muscle is separated from the short head. The fascia lata is stripped up to the insertion of the gluteus maximus muscle laterally, and the medial edge is freed up to the tensor fasciae femoris. A sheath is made of the remaining fascia lata to serve as a guide for the transplants. At the patella, insertion is made by two drill holes. Massage and muscular reeducation are begun the fifth week after operation. Braces are usually worn for six to eight weeks for walking. The operation is described in detail and illustrated with line drawings.

Opposition of the Thumb.—In an excellent and well illustrated article Bunnell³³ describes the "opposition" and goes into detail regarding the range of motion of the thumb. After naming the causes of

30. Ober, F. R., and Barr, J. S.: Surg., Gynec. & Obst. 67:105, 1938.

31. Yount, C. C.: J. Bone & Joint Surg. 20:314, 1938.

32. Yount, C. C.: J. Bone & Joint Surg. 8:171, 1926.

33. Bunnell, S.: J. Bone & Joint Surg. 20:269, 1938.

loss of opposition he describes methods of its restoration. He feels that there are two essential principles of tenoplasty. First, the tendon from its insertion in the thumb should be passed subcutaneously in the direction of the pisiform bone, so that it will pull the thumb in the correct direction, and second, the insertion of the tendon should be on the dorsoulnar aspect of the face of the proximal phalanx of the thumb, so as to restore the pronatory component. He also mentions briefly other methods of restoring opposition of the thumb, as described by other authors. The operative technic advocated adheres to the two essential principles mentioned. For motor power the flexor carpi ulnaris tendon, the palmaris longus tendon, the flexor digitorum sublimis tendon of the ring finger or any of the available long flexor muscle tendons may be used. The extensor carpi radialis brevis tendon or the palmaris longus tendon may be prolonged sufficiently by use of its prolongation, the palmar fascia, or any tendon desired can be pieced out by a free tendon graft either from the palmaris longus tendon or from any other tendon available. For the construction of a pulley at the pisiform bone, a free tendon graft from the palmaris longus or from any other available tendon can be looped around the short muscle and tendon attachment to the pisiform bone and sutured to itself, so that it forms a circle 2 cm. in diameter. The sutured junction is then slipped around until it is within the muscle. Instead of constructing a pulley one may pass the tendon used around the flexor carpi ulnaris tendon and on to its insertion in the phalanx of the thumb. For the sake of clarity, Bunnell's technic is shown in line drawings and photographs.

Treatment of Athetosis by Section of the Extrapyramidal Tract.—Putnam³⁴ reports 27 cases in which section of the extrapyramidal tracts in the spinal cord was done. Twenty-three of the patients were suffering from the "athetoid syndrome." Of these, 17 showed varying degrees of improvement. There were 3 postoperative deaths. In 4 of the 27 cases there was no improvement. On further analysis the patients in these cases were found to be of a different type from those with the "athetoid syndrome." The tremor was of a type of which paralysis agitans is the familiar example. In the series of 23 patients 12 were female and 11 male. The ages varied from 8 to 56. Thirteen had bilateral athetosis. Twelve had normal or superior mentality and 15 had a history of difficult delivery. The operation is carried out as high as possible, usually at the second cervical interspace. It consists of cutting the nonpyramidal motor pathways which lie in the anterior quadrant of the spinal cord, consisting of the vestibulospinal, reticulospinal and

34. Putnam, T. J.: Results of Treatment of Athetosis by Section of the Extrapyramidal Tracts in the Spinal Cord, *Arch. Neurol. & Psychiat.* 39:258 (Feb.) 1938.

tectospinal pathways, with perhaps a few corticospinal fibers. If torticollis is present the operation is combined with section of the first three anterior roots. Putnam stresses the danger of operating on more than one side of the cord at one time.

Durham³⁵ found that marked internal rotation of the thigh in cases of cerebral spastic paralysis was not relieved by division of the adductor and flexor muscles and lengthening of the hamstrings but was relieved by division of those parts of the gluteus muscles which are attached anterior to the tip of the greater trochanter as well as by division of the tensor fasciae latae muscle. For this procedure a short diagonal cutaneous incision is made from behind immediately forward over the greater trochanter. Immobilization in plaster is used to maintain the thigh in abduction and full external rotation for six to eight weeks. Thirty-two operations of this nature have been performed on 20 patients in the past six years, with correction maintained in all cases.

Posterior Radicotomy for Spastic Paralysis.—Yovtchitch³⁶ speaks in defense of Foerster's operation, resection of the posterior nerve roots, in cases of severe spastic paralysis. He emphasizes the importance of muscular reeducation for all spastic patients. Tenotomy and the Stoffel operation should be utilized only for the milder forms of spasticity. The author expresses disagreement with those who feel that resection of the posterior nerve roots is too severe an operation for the spastic child to undergo. He has done 7 operations on 6 patients since 1925. Some of the operations have been cervical and some lumbar, and no untoward complications have followed any of them. It must be ascertained before operation that the child has sufficient intelligence to undertake post-operative muscular reeducation, and this sometimes requires a long period of observation. The author states that in every case the spasticity has subsided immediately after the operation, and in 1 case of athetosis the movement ceased. The results after several years of follow-up appear to be permanent. The author believes that no other procedure at present can equal the Foerster operation for severe spastic conditions.

[ED. NOTE.—This procedure has been given up almost entirely in America. It will be interesting to follow the author's opinion after he has had wider experience with this operation.]

FRACTURES

Fracture of the Atlas in Automobile Accidents.—Plaut³⁷ has added 6 cases of fracture of the atlas to the 93 recorded in the literature. The

35. Durham, H. A.: J. Bone & Joint Surg. 20:339, 1938.

36. Yovtchitch, M.: Presse méd. 46:689, 1938.

37. Plaut, H. F.: Fracture of the Atlas in Automobile Accidents: The Value of X-Ray Views for Its Diagnosis. J. A. M. A. 110:1892 (June 4) 1938.

injury was due to force transmitted through the top of the skull (the patient's head hitting the top of the car) to the atlas with the head in an erect position. This force fell on the curved facets, breaking the ring of the atlas at the anterior or posterior arch. Roentgen technic and diagnosis are discussed. Injury to the spinal cord is rare, and treatment consists of immobilization for considerable time because of slow osseous repair.

Isolated Fractures of the Vertebral Arch.—Steiner³⁸ presents several cases of isolated fracture of the vertebral arch, particularly in the lumbar portion of the spine. Such fracture is observed in the articular processes, the interarticular portion or the pedicle. It may result from mild trauma and may explain some obscure forms of pains in the sacral region. Treatment is not described.

Valgus Position for Fractures of the Hip.—Cotton and Morrison³⁹ state that although it is well recognized that vastly better results are obtained in cases of intracapsular fracture of the neck of the femur if the displacement happens to be in the valgus position, it is only recently that they have learned how to produce this valgus position at will. Lateral roentgenograms of the hip have made it possible to determine the previously overlooked factor of forward rotation of the proximal end of the distal (neck) fragment. The procedure used by the authors is traction in the line of the femur, the hip and knee being moderately flexed; sharp adduction; crossing of the broken limb, followed by sound side, and sharp inward rotation of the knee over the thigh of the bringing down of the leg into slight abduction (about 20 degrees) without relaxation of the inward rotation. The results are then checked by anteroposterior and lateral roentgenograms. If they are not satisfactory the maneuver is repeated. If satisfactory position is attained the leg is abducted 20 or 30 degrees from the midline of the body, and a heavy wooden mallet is used to impact the fracture; a heavy layer of felt is placed over the greater trochanter, which is struck in line with the neck of the femur, the hammer being kept parallel with the degrees. This brings the femoral neck into an angle of from 105 to 110 with the shaft. After reduction and impaction the fragments are nailed with Krupt nails, holes having been drilled under fluoroscopic control. The nails are then tapped home. The death of the femoral head, which occurs occasionally, is still a mystery and cannot be controlled by this method any better than by any of the others. However, the authors feel that should aseptic necrosis ensue, the valgus position is the posture in which the bone may best resist this misfortune. Excellent roentgenograms and line drawings are included in this article.

38. Steiner, G.: Am. J. Roentgenol. 39:43, 1938.

39. Cotton, F. J., and Morrison, G. M.: J. Bone & Joint Surg. 20:46, 1938.

Central Fracture of the Neck of the Femur.—Campbell and his associates⁴⁰ have operated in 49 cases of complete central or intra-capsular fracture of the neck of the femur, employing the three-flanged nail to secure internal fixation. Twenty-nine patients have been followed for over one year. Of these, 88 per cent are reported to show solid union. However, 9 per cent show degenerative changes indicative of devitalization of the femoral head, with an ultimate prognosis of poor function. Campbell states that internal fixation materially decreases the time in which union is secured, conserves the function of the hip and knee and decreases the mortality by reason of the less extensive means of immobilization and the shorter confinement to bed.

Fracture of the Neck of the Femur Treated by Oblique Osteotomy.—McMurray⁴¹ reviews the method of Whitman and that of Smith-Petersen for the treatment of transcervical fracture. With Whitman's method union may be expected in 50 to 60 per cent of cases. With Smith-Petersen's method 70 to 80 per cent of patients obtain union, but of these about one fourth have aseptic necrosis of the femoral head within four or five years. Oblique osteotomy was first performed in 27 cases of nonunion of the neck of the femur and later was tried in 4 cases of recent fracture. In all these cases the result was satisfactory, the only deformity being a shortening of $\frac{1}{2}$ to $\frac{3}{4}$ inch (1.2 to 1.9 cm.) and the only limitation being inability to adduct the leg across the middle line. The operation consists of osteotomy of the shaft of the femur just below and parallel to the lower border of the neck of the femur. The shaft is displaced inward, the cut surface of the shaft being brought close beneath the line of fracture through the neck and beneath the lower border of the acetabulum. The limb is enclosed in a plaster spica in the neutral position. Callus formation extends from the shaft into the cervical fracture line, fusing all three fragments and giving a stable, painless hip with good range of motion, limitation being present only in adduction.

Ambulatory Method of Treating Fracture of the Femoral Shaft.—Anderson⁴² describes a further elaboration of his apparatus⁴³ for fixation of fracture of the femoral shaft. The half pins are placed through the femoral shaft at an angle, and their protruding ends are connected by a bar. Two pins, also at an angle, are drilled through the femoral condyles from the inner side. After the fracture has been reduced, the thigh, with the upper and the lower pin, is incorporated in plaster. The entire procedure is usually carried out on a fracture

40. Campbell, W. C.: *Minnesota Med.* **21**:260, 1938.

41. McMurray, T. P.: *Brit. M. J.* **1**:330, 1938.

42. Anderson, R.: *Am. J. Surg.* **39**:538, 1938.

43. Anderson, R.: *J. Bone & Joint Surg.* **16**:379, 1934.

table. Roentgenograms are taken to secure fixation in proper position. The plaster is trimmed at the groin and at the knee to permit motion at the knee and hip joints. Walking is permitted as soon as the plaster is dry and the general condition of the patient permits. There is usually no pain. The apparatus is removed as a rule in eight to twelve weeks.

Fractures of the Elbow in Children.—Robertson⁴⁴ reviews the general principles governing the treatment of fractures of the elbow. He advises immediate reduction to prevent unnecessary pain and to improve circulation. No sedative should be given without certainty that normal circulation is present in the fingers. For fracture involving the articular surface, a perfect reduction, by open operation if necessary, is essential.

Fractures of the Forearm.—Kotrnetz⁴⁵ lists the results of treatment for fracture of the forearm in the Second Surgical University Clinic in Vienna, Austria, considering the material in two divisions, fractures in children and fractures in adults. The methods of Boehler were regularly employed. The data for the first group are as follows: One hundred and eight fractures in the distal third of the radius were treated. Only those with more than 15 per cent of angulation were subjected to reposition. An average of twenty-seven days in a short arm plaster cast was employed. In 3 cases there was refracture after removal of the plaster in three weeks. There were 24 cases of fracture of the middle and the proximal third of the radius; in 21 reduction was done; forty-three days was the average period of immobilization, which was obtained principally by plaster casts including the elbow. In 1 case there were circulatory difficulties despite early splitting of the plaster, and in 2 cases refracture occurred in spite of long fixation. Eleven arm plaster cast for an average of thirty-one days. In 2 cases refracture occurred after four weeks of immobilization. One case, in which healing had occurred with considerable lateral displacement of one fragment, was reviewed five years after the original fracture. No sign of the displacement or the site of fracture was demonstrable. Greenstick fracture of both bones in the distal third was treated with both short and long arm plaster casts in 68 cases. An average of twenty-four days' immobilization was employed. In 57 cases reduction was required. In 4 of these a second reduction was necessary after ten to fourteen days, and in 1 there was refracture four weeks later because there was loss of 20 per cent of supination and slight (less than 15 per cent) axial deformity; in 2 cases refracture occurred after removal of the plaster. Subperiosteal or greenstick fracture in the middle and the

44. Robertson, D. E.: Am. J. Surg. 39:327, 1938.

45. Kotrnetz, H.: Arch. f. orthop. u. Unfall-Chir. 38:673, 1938.

proximal third of both bones was treated in 111 cases, the average period of immobilization (in a long arm plaster cast) being forty-eight days. Three patients were left with mild angulation and lost 30 per cent of supination. Otherwise the end results were excellent. A striking feature was the fact that there were 14 cases of circulatory disturbance requiring splitting of the plaster and 4 cases in which refracture occurred. Two fractures with punctures of the skin healed without complication. In 36 cases of fracture of the distal third of both bones with lateral displacement the average period of immobilization in plaster was forty-six days. Eight temporary circulatory disturbances were noted; 4 resulted in slight radial angulation of 1 in a loss of 20 degrees of supination. Of 40 fractures of both bones in the middle and the proximal third of the forearm with lateral displacement, 37 were reduced by the close method and 3 required the use of operative methods (2 being treated by double wire traction and 1 by plating with the Lane plate). Thirteen fractures were reduced under the fluoroscope. The average period of immobilization was fifty-seven days. The end results were good. In 5 cases there was slight dorsal angulation and in 3 a 20 per cent loss in supination. In summary, of these 398 fractures in children treated by unpadded plaster, it may be said that the results are excellent. The author explains the occurrence of circulatory disturbance in 32 cases as caused by the development of a secondary, operatively produced hematoma during the manually produced fracture of the remaining cortex in correction of greenstick deformities. He believes delaying reduction for twenty-four hours will help for greenstick lesions but that early reduction will help most for lesions with lateral displacement. He notes the frequency of refracture in children and advises continued guarding even after roentgenographic union has occurred.

The data in the second group are as follows: Of 34 fractures of the radius in the middle and the proximal third, 26 required reduction; 1 required open reduction. There were 6 circulatory disturbances; 1 untreated for four days, ended disastrously. In the study of end results, 4 presented limitation of pronation and supination. All were treated simply by fixation in plaster (long arm cast) even if the distal ulnar-radial ligaments were torn. The hand was fixed in supination for fractures of the proximal third and in midposition for fractures of the distal third. Of 24 fractures of the ulnar shaft union was obtained after an average of fifty-eight days' fixation in plaster (long arm cast). Only 5 had showed any displacement. Of 30 fractures of the shafts of both bones, 17 were treated by fixation, 8 by double wire fixation and 5 by open operation. Aside from the cosmetic inferiority of the results in cases in which casts were used, the results statistically seem as good as in those in which wire extension was used.

[ED. NOTE.—This large series of fractures of the forearm treated for the most part by simple means suggests that careful supervision through the entire period of healing is the best guarantee of a satisfactory result.]

Fracture Disabilities of the Forearm.—Steindler⁴⁶ reviews the disabilities following fracture of the forearm. He lists these under (1) malalignment of Colles' fracture, (2) nonunion of fracture, (3) arthritis of the wrist joint and (4) soft tissue contractures. These common disabilities can be largely prevented by more perfect reduction of the fracture. Disturbances of the nerves and circulation are not always preventable. Early repair of neural lesions, judicious physical therapy, adequate splinting, elevation of the forearm, freedom of the fingers, passive motion and subsequent exercises are of greatest importance.

Injuries to the Triangular Ligament of the Wrist.—Guillermo⁴⁷ stresses the fact that injuries to the triangular ligament of the wrist often are unrecognized and may lead to persistent disability. The ligament is biconcave and acts as an elastic cradle for the head of the ulna. It originates from two roots, one from the inferior surface of the radius and the other from the small sigmoid cavity of the radius, and extends horizontally beneath the head of the ulna to terminate in two roots, one on the external aspect of the ulnar styloid process and the other between the styloid process and the head of the ulna. During supination and pronation the radius rotates around the axis, passing through the head of the ulna. During these movements the triangular ligament acts as a shock absorber and takes the pressure of the hand from the ulnar head. During a fall on the hand with the wrist in pronation the ligament is put on the stretch and prevents separation of the radius and the ulna. An osseous injury to the lower part of the radius or the ulna may involve the triangular ligament, but injury to the ligament may also occur in the absence of osseous injury. Hence, roentgenographic integrity of the bones does not necessarily mean that the ligament has not been damaged. Clinical signs of injury to the ligament may be present. With rupture of the ligament there may be dorsal displacement of the ulna, and if this has occurred the head of the ulna may be moved up and down by pressure with the thumb. This sign has no significance in children because of the flexibility of the ligament. In the presence of an old lesion there may be crepitus in the wrist on motion, or a definite click may be felt as the head of the ulna is pushed into place. Pain and limitation of supination and pronation may result from separation of the radius and the ulna. In case of persistent disability the author advises removal of the triangular ligament.

46. Steindler, A.: J. Connecticut M. Soc. 2:163, 1938.

47. Guillermo, J.: Rev. d'orthop. 25:125, 1938.

Fractures of the Scapula and Ribs.—Findlay⁴⁸ reviews 37 cases of fracture of the scapula and 163 cases of fracture of the ribs. In 25 of the scapular fractures there were associated bony injuries in other parts of the body. Associated fractures of the ribs were most common. The body of the scapula was the most commonly fractured, this being the site of fracture in 29 cases. Other fractures were distributed as follows: glenoid fossa, 7; acromion, 4; spine, 2; neck, 2; coracoid process, 2. The treatment is rest in bed and support, usually followed by heat, massage and exercise of the shoulder after the first week. Open reduction was attempted in 1 case but was unsuccessful. Incomplete fractures were treated with a sling, and the patients were allowed to walk. Four of these patients died in the hospital from multiple injuries. Of 12 that could be traced, 8 showed good results, 3 fair results and 1 a poor result. Most of these fractures occurred in middle-aged laborers. The ribs most frequently fractured were the fifth, sixth and seventh. The first and the twelfth were least often broken. Forty of the patients died in the hospital from associated injuries. Among these there were 5 with laceration of the lung, 6 with hemothorax and 6 with hemothorax. The common form of treatment was strapping with adhesive plaster. The end results in 25 of 32 cases were good; 7 patients had persistent pain. When there is severe respiratory embarrassment with fracture of the ribs, unrelieved by strapping, the administration of oxygen is advocated. For hemothorax the author suggests, but has not tried, aspiration and replacement of the fluid with sterile air. An increase in temperature to 104 or 105 F. after a slight, constant fever in the presence of pleural effusion or hemothorax suggests the probable presence of empyema.

Treatment of Slipping of the Upper Femoral Epiphysis.—Wilson⁴⁹ discusses two points: (1) the treatment of early stages of slipping of the upper femoral epiphysis, and (2) the effect of operative fusion of the upper femoral epiphysis on growth of the lower extremity. Early treatment requires alertness on the part of the physician to make a correct diagnosis. In this case of a patient between the ages of 10 and 16 years, complaining of intermittent pain and stiffness in the knee or thigh, with at times a noticeable limp, one should consider slipping of the epiphysis as one of the first possibilities. In approximately 70 per cent of cases the patient is overweight. Roentgen examination reveals irregular rarefaction of the metaphysial zone of the neck in immediate contact with the epiphysial cartilage, giving a characteristic appearance of widening of the epiphysial line. This is always evident, especially on comparison with the normal hip. The author believes that

48. Findlay, R. T.: *Am. J. Surg.* 38:489, 1937.

49. Wilson, P. D.: *J. Bone & Joint Surg.* 20:379, 1938.

real slipping occurs as soon as the epiphysis is loosened. Without slipping it is doubtful if there would be any symptoms. A lateral roentgenogram usually gives more information than an anteroposterior one. Treatment consists of fixation as soon as a diagnosis is made. With the patient under general anesthesia an incision is made over the lateral aspect of the trochanter, and the Smith-Petersen nail is started at a point about 1 inch (2.5 cm.) below the ridge for the insertion of the vastus lateralis muscle. The leg is held by an assistant with the hip internally rotated as much as possible, and the nail is driven home at the angle and to the depth previously determined from measurements of the roentgenogram of the hip. Arthrotomy of the hip joint is not necessary, and replacement of the slightly displaced head is not necessary unless the head has slipped off more than one third of the diameter of the neck of the femur. Fusion of the upper femoral epiphysis has shown that serious shortening of one extremity does not result. Certainly growth from the epiphysis has been known to stop when nailing or drilling through this region is done, but follow-up studies in 9 cases revealed no increase in the amount of shortening after the operation. Closure of the unaffected epiphysis usually takes place within two years after the occurrence of slipping, which is frequently considerably in advance of the normal time. The author gives complete histories of the 9 cases reported, showing roentgenograms, pictures and photographs of the patients.

After-Care of Fracture.—In the after-care of fracture, Hoke and his associates⁵⁰ advise roentgen examination of reduced fractures once a week until there is sufficient union to prevent slipping. In the healing of fractures there should be no pain. Pain is usually the result of undue pressure on the body from the retaining apparatus. All apparatus should be so arranged by skeletal plaster fixation or skeletal plaster traction that the patient can be moved from his bed to a wheel chair daily. Compound fractures, after cleaning and reduction, are packed with petrolatum gauze to permit drainage and healing of the wound. Motion in the joints adjacent to a fracture should be begun when there is sufficient callus to prevent displacement of the fragments. Firm union of the fractured bone, however, is more important than articular motion. For recovering motion in a joint, heat, massage and the galvanic current are of value. The authors describe simple splints to protect the site of fracture when use is first resumed.

Functional Disabilities After Simple Fracture.—Gurd⁵¹ discussed disabilities arising from simple fracture and not due to easily recognized causes, such as shortening, angulation or nonunion. He suggests that

50. Hoke, M.; Thornton, L., and Sandison, C.: *J. M. A. Georgia* 27:10, 1938.

51. Gurd, F. C.: *Surg., Gynec. & Obst.* 66:489, 1938.

disability following apparently uncomplicated fractures is often due to osseous atrophy and associated changes in tendons and ligaments. The chief cause for such atrophy, he concludes, is hyperemia. This hyperemia persists because of irritation at or about the site of fracture. The main causes of such irritation are: (1) inadequate fixation, and (2) short period of absolute fixation to prevent atrophy. Adequate fixation of sufficient duration should be employed, and at the same time function should be established as completely and easily as possible; i. e., with fracture of the lower extremity protected weight bearing should be begun, and in the upper extremity there should be absolute fixation of the area of fracture with as great freedom as possible for the hand and fingers.

Functional Disabilities after Simple Fracture.—Every fracture should be regarded as a potential source of permanent disability, according to Henderson.⁵² He mentions the posterior deformity of the wrist caused by Colles' fracture, the posterior displacement caused by supracondylar fracture of the humerus and the sometimes associated Volkman's contracture. At the ankle joint the common deformities are nonunion of the internal malleolus, valgus deformity and valgus deformity with posterior displacement. At the hip joint, nonunion of fracture of the femoral neck is the most common. Physical therapy and methods of correcting these deformities are discussed.

RESEARCH

Influence of the Sympathetic Nervous System on Healing of Fractures.—Lexer⁵³ first reviews the literature on sympathectomy. He then recounts the findings of Wassiljeff and Scholondz,⁵⁴ who noted marked differences in homoplastic graft healing in sympathectomized dogs. Using rabbits, Lexer repeated the experiments. He found that while the leg operated on was apparently stimulated to repair the defect faster than it was repaired on the normal side, no true healing of the transplant to its base took place. In 34 sympathectomized animals and 21 controls the author studied callus formation after manually fracturing the femur. At various stages of healing the animals were killed, and the vascular network of the callus was visualized roentgenographically by injection of opaque mediums. Histologic sections were also prepared. It appeared that although the callus was larger in the sympathectomized animals, union of the fracture was always slower. While sympathectomy may speed up callus formation in cases of delayed union, it is clinically uncertain and dangerous. In the presence of true pseudarthrosis sympathetic division is completely without value.

52. Henderson, M. S.: Arch. Phys. Therapy **19**:7, 1938.

53. Lexer, E. W.: Deutsche Ztschr. f. Chir. **249**:337, 1937.

54. Wassiljeff, A. A., and Scholondz, A. M.: Arch. f. klin. Chir. **178**:148, 1933.

Diffraction Studies on Human Bone.—Reynolds, Hayden and Corrigan⁵⁵ present an interesting preliminary report on roentgen ray diffraction patterns of bone and quantitative chemical analyses. They have found that diffraction patterns of bone from patients with Paget's disease and normal bone show an apatite (calcium phosphate fluoride or calcium phosphate chloride) structure. Diffraction patterns of bone from a patient with parathyroidism show a structure different from apatite.

Pathogenesis of Perthes' Disease.—Nagura and Kosuge⁵⁶ ingeniously reproduced experimentally the early changes of Legg-Perthes disease in rabbits. Using rabbits 4 weeks old, the authors exposed the hip and with a sharp knife produced a "traumatic injury" to the epiphysal plate. The animals were allowed to walk around normally and were killed in three to thirty-six days after operation. The changes were studied grossly and microscopically. The immediate picture showed only separation where the knife had entered. Later there was regeneration, consisting of chondrogenesis and spongiogenesis. Secondary clefts arose in the epiphysal plate and articular cartilage. There was deformity, usually flattening of the femoral head. The lesions were progressive, and the authors believed that complete healing did not occur while the animal walked around. The authors concluded, after discussing the various theories of the causation of Legg-Perthes disease (infection, infectious osteochondritis, bony necrosis and mycotic emboli), that the condition is due to minor injuries to the head of the femur. Weight bearing as long as the injury is not healed causes irregular growth. The fact that a history of injury is only rarely obtained indicates that the patients do not remember incidents of slight trauma.

Round Ligament and Vascularization of the Femoral Head.—This study was undertaken by Nordenson⁵⁷ to determine the presence and caliber of arteries in the ligamentum teres in patients of different age groups. The material comprised 129 normal hips, the ages of the patients ranging from infancy to 90 years, with a good distribution in the various decades. Twenty patients with intracapsular fractures of the femoral neck also were examined. The method of study consisted of excision of the entire ligamentum teres, including a portion of the adjacent head of the femur. The specimens were then fixed and cut into serial sections for histologic study. The arteries were not injected, the author concluding that this procedure is apt to lead to false results. In 91 of the 129 normal ligaments, vessels of fair size were

55. Reynolds, L.; Hayden, H. S., and Corrigan, K. E.: *Am. J. Roentgenol.* 39:286, 1938.

56. Nagura, S., and Kosuge, S.: *Arch. f. klin. Chir.* 191:347, 1938.

57. Nordenson, N. G.: *Lyon chir.* 35:178, 1938.

easily traced into the femoral head. In 14 cases no vessel or only very feeble vessels were found. In 24 cases there were vessels in the proximal part of the ligament, which, however, soon broke up into small branches and were difficult or impossible to trace into the head. In 15 cases vessels had been obliterated by arteriosclerosis. Arteries in the ligament were observed in specimens from all age groups, but in those from the higher age groups vessels were more frequently lacking or small or had been obliterated by arteriosclerosis. The blood supply, when present, was never by a single artery but always by several small arteries. Vessels were demonstrated in each of the 20 cases in which intracapsular fracture had occurred. It is interesting to note that in nearly all of these the vessel was of larger caliber than those found in the normal hip, indicating an ability of the arteries to adapt themselves to the increased demand for blood in the femoral head.

Anatomy of the Sternoclavicular Joint.—Remarking on the paucity of reports on the sternoclavicular joint, Rathcke,⁵⁸ after reviewing the standard anatomic descriptions describes his findings in various specimens classified according to age. He observes that more often than not the two joint compartments formed by the intra-articular disk communicate at one point. The fibers of the disk in youth have a regular pattern, and blood vessels are visible only peripherally. With advancing age the pattern becomes less clear. The disk is fragmented in places and becomes stained a yellowish color (this is similar to Schmorl's observations on the intervertebral disks). No synovial lining was found. The occurrence of effusion in the joint, therefore, is questioned by Rathcke. With advancing age, just as the disk undergoes attritional changes similar to those seen in the meniscuses, the component joint surfaces of the clavicle and the sternum lose gradually their hyaline cartilage.

58. Rathcke, L. D.: *Ztschr. f. Chir.* **249**:162, 1938

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